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(54) **NUCLEIC ACIDS USEFUL FOR INTEGRATING INTO AND GENE EXPRESSION IN HYPERTHERMOPHILIC ACIDOPHILIC ARCHAEA**

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C12N 9/42 (2006.01)

(52) **U.S. Cl.**
CPC ***C12N 9/2437*** (2013.01); ***C12N 15/74*** (2013.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

8,580,543	B2	11/2013	Burk et al.
2007/0134201	A1	6/2007	Schleper
2010/0209986	A1	8/2010	Liao et al.

FOREIGN PATENT DOCUMENTS

KR	20080055552	A	6/2008
WO	2012/064195	A2	5/2012

OTHER PUBLICATIONS

Albers et al., "Conditions for gene disruption by homologous recombination of exogenous DNA into the *Sulfolobus solfataricus* genome," Archaea, 2:145-149 (2007).
Albers, et al., "Production of Recombinant and Tagged Proteins in the Hyperthermophilic Archaeon *Sulfolobus solfataricus*," *Applied And Environmental Microbiology*, 72(1):102-111 (Jan. 2006).
Barthelme, et al., "Structural Organization of Essential Iron-Sulfur Clusters in the Evolutionarily Highly Conserved ATP-binding Cassette Protein ABCE1," *Journal of Biological Chemistry*, 282(19):14598-14607 (2007).
Bouabe et al., Nucleic Acids Research, 2008, 36(5):1-9.
GenBank Accession No. AE006641 (Apr. 24, 2001).
Extended European Search Report from European Patent Application No. 13856207.9, dated Jun. 30, 2016.
Peng, "An upstream activation element exerting differential transcriptional activation on an archaeal promoter," *Molecular Microbiology*, 74(4) pp. 928-939 (2009).
Ghosh, et al., "Archaeal flagellar ATPase motor shows ATP-dependent hexameric assembly and activity stimulation by specific lipid binding," *Biochem. J.*, 437:43-52 (2011).
Jonuscheit, et al., "A reporter gene system for the hyperthermophilic archaeon *Sulfolobus solfataricus* based on a selectable and integrative shuttle vector," *Molecular Microbiology*, 48(5):1241-1252 (2003).
Peng, "Evidence for the horizontal transfer of an integrase gene from a fusellovirus to a pRN-like plasmid within a single strain of Sulfolobus and the implications for plasmid survival," *Microbiology*, 154:383-391 (2008).
Pisani, et al., "Thermostable Beta-galactosidase from the archaebacterium *Sulfolobus solfataricus* Purificationa nd properties," *Eur. J. Biochem.*, 187:321-328 (1990).
Stedman, et al., "Genetic Requirements for the Function of the Archaeal Virus SSV1 in Sulfolobus solfataricus: Construction and Testing of Viral Shuttle Vectors," *Genetics*, 152: 1397-1405 (Aug. 1999).
The International Search Report and Written Opinion from PCT/US2013/071328, dated Feb. 27, 2014.

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(74) *Attorney, Agent, or Firm* — Kilpatrick Townsend & Stockton LLP

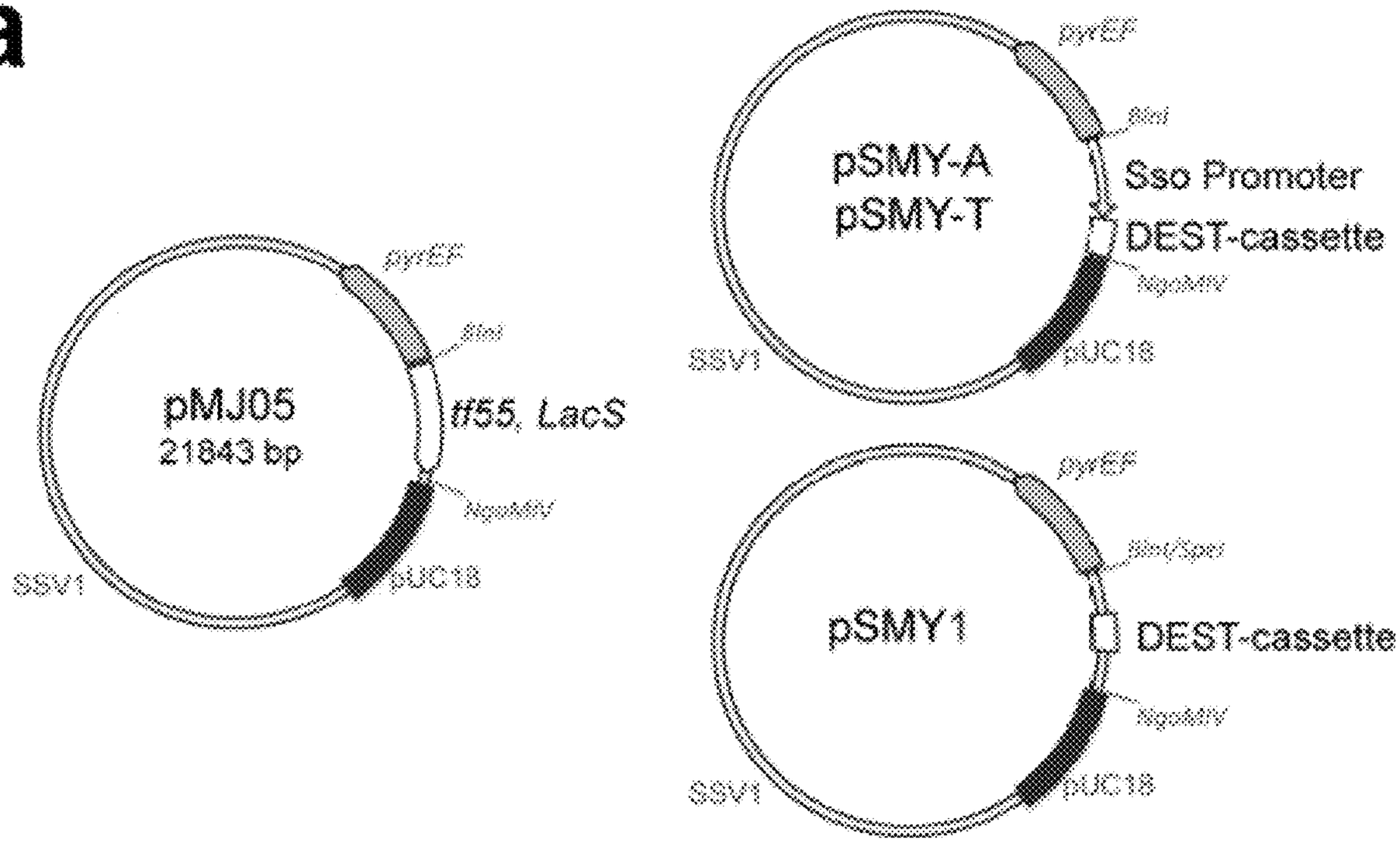
(57) **ABSTRACT**

The present invention provides for a novel recombinant or isolated nucleic acid useful for integrating or being maintained in an Archaea or acidophilic hyperthermophilic eubacteria. The nucleic acid encodes a nucleotide sequence that is capable of stably integrating into the chromosome of a host cell, or being maintained as an extrachromosomal element in a host cell, that is an Archea, and a nucleotide sequence of interest. The present invention also provides for an Archaea host cell comprising the nucleic acid stably integrated into the chromosome or maintained episomally in the host cell, and a method of expressing the nucleotide sequence of interest in the host cell and/or directing glycosylation, multimerization, and/or membrane association or integration.

15 Claims, 10 Drawing Sheets

Specification includes a Sequence Listing.

a


pMJ05
21843 bp
tf55, LacS
SSV1
pUC18
pSMY-A
pSMY-T
Sso Promoter
DEST-cassette
pSMY1

b

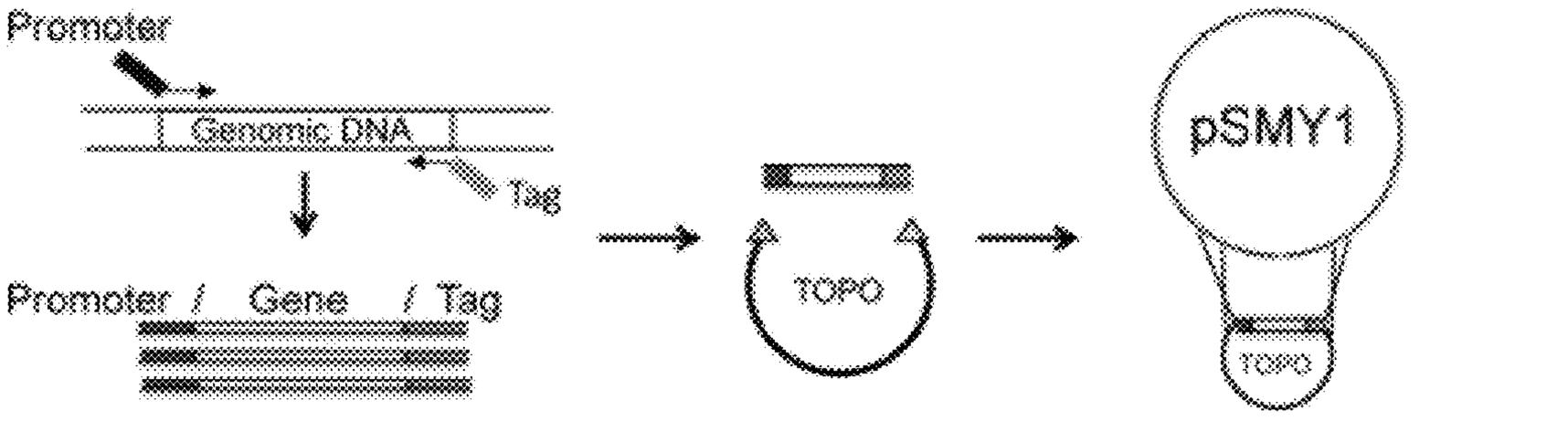

Promoter
Genomic DNA
Tag
Promoter / Gene / Tag
TOPO
pSMY1
1) PCR Amplification
2) TOPO-Cloning
3) In Vitro Recombination

Figure 1

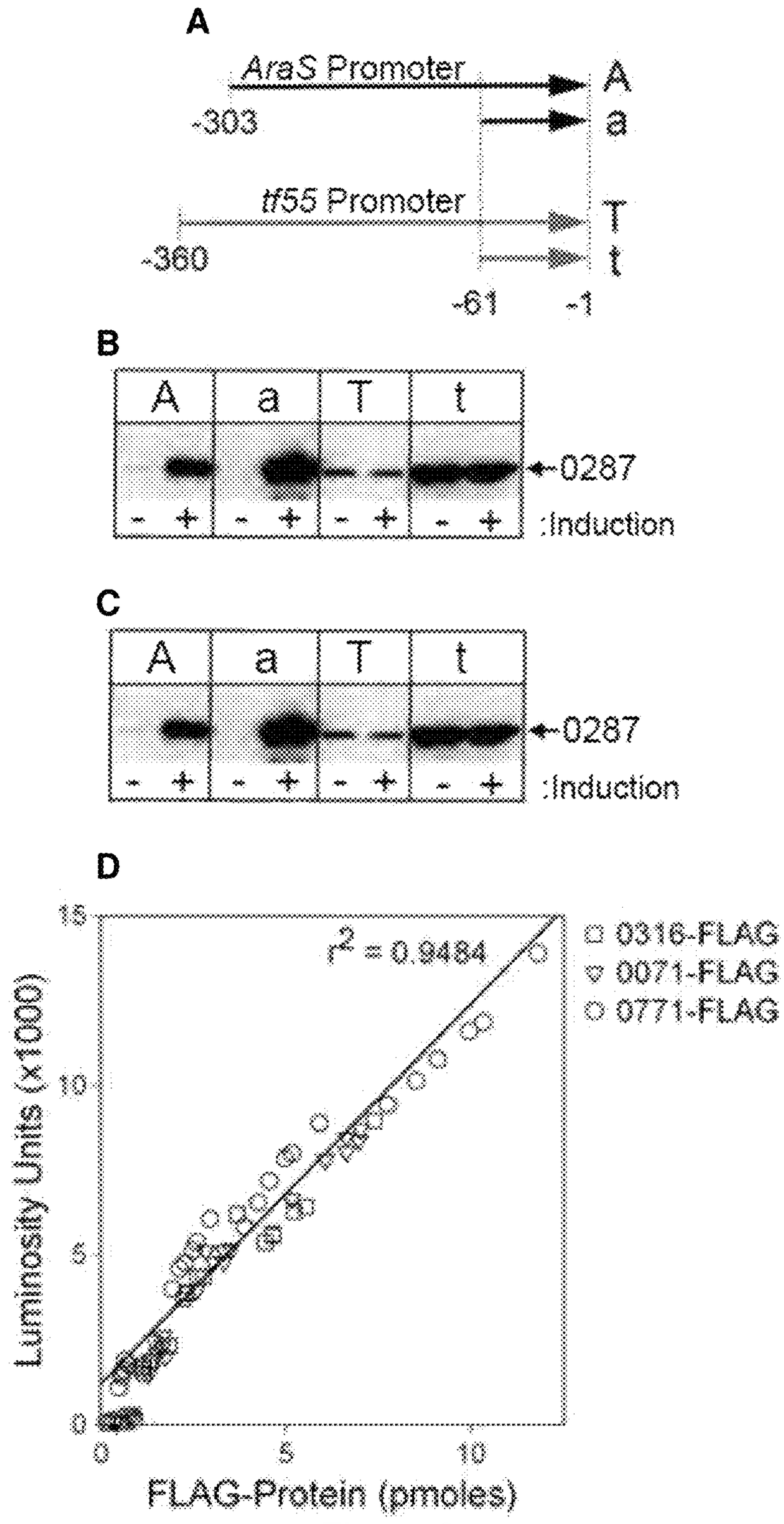

A
AraS Promoter
A
-303
a
tf55 Promoter
T
-360
t
-61
-1
B
A
a
T
t
0287
- + - + - + - +
:Induction
C
A
a
T
t
0287
- + - + - + - +
:Induction
D
15
10
5
0
0
5
10
r^2 = 0.9484
Luminosity Units (x1000)
FLAG-Protein (pmoles)
0316-FLAG
0071-FLAG
0771-FLAG

Figure 2

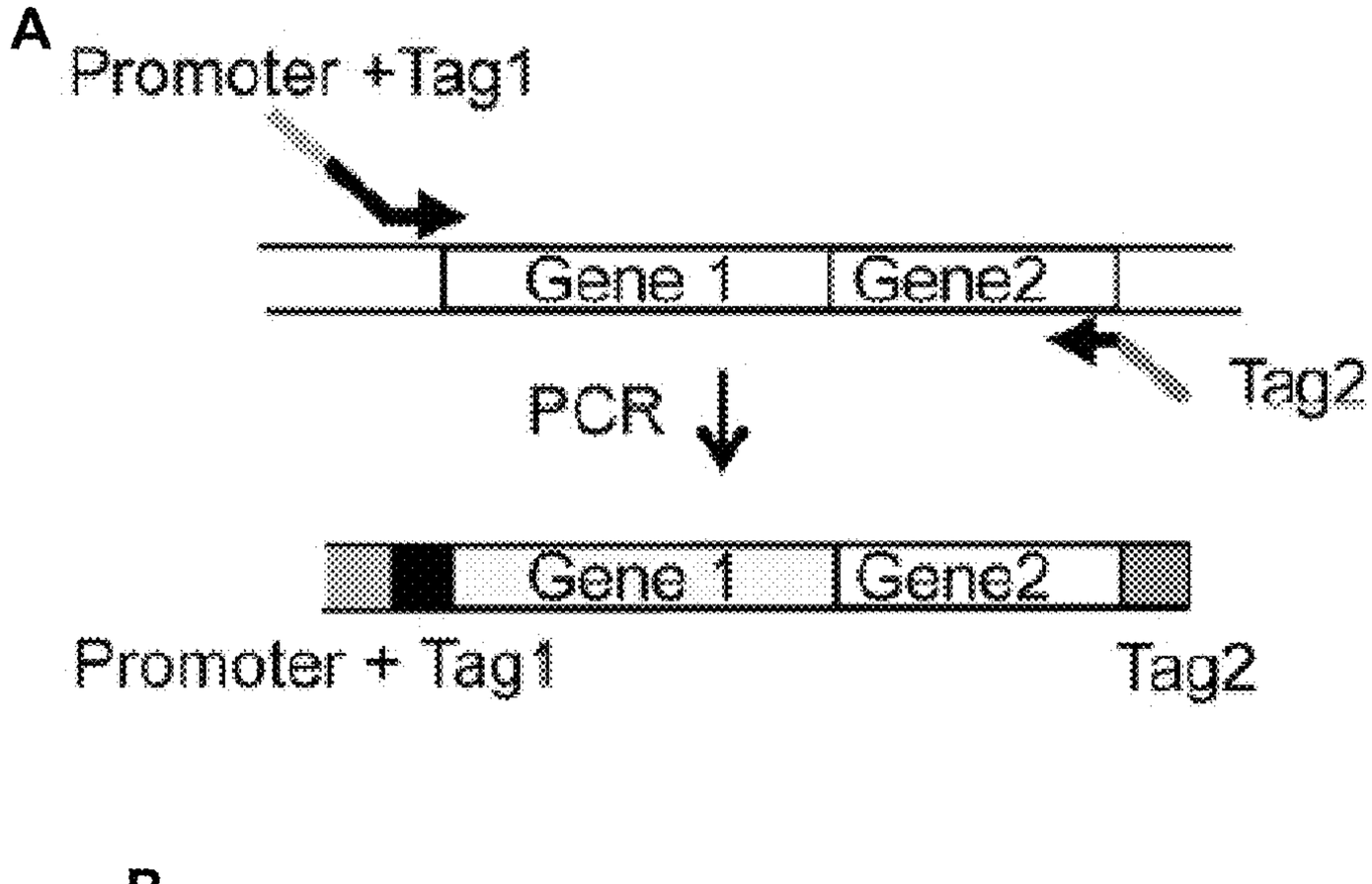
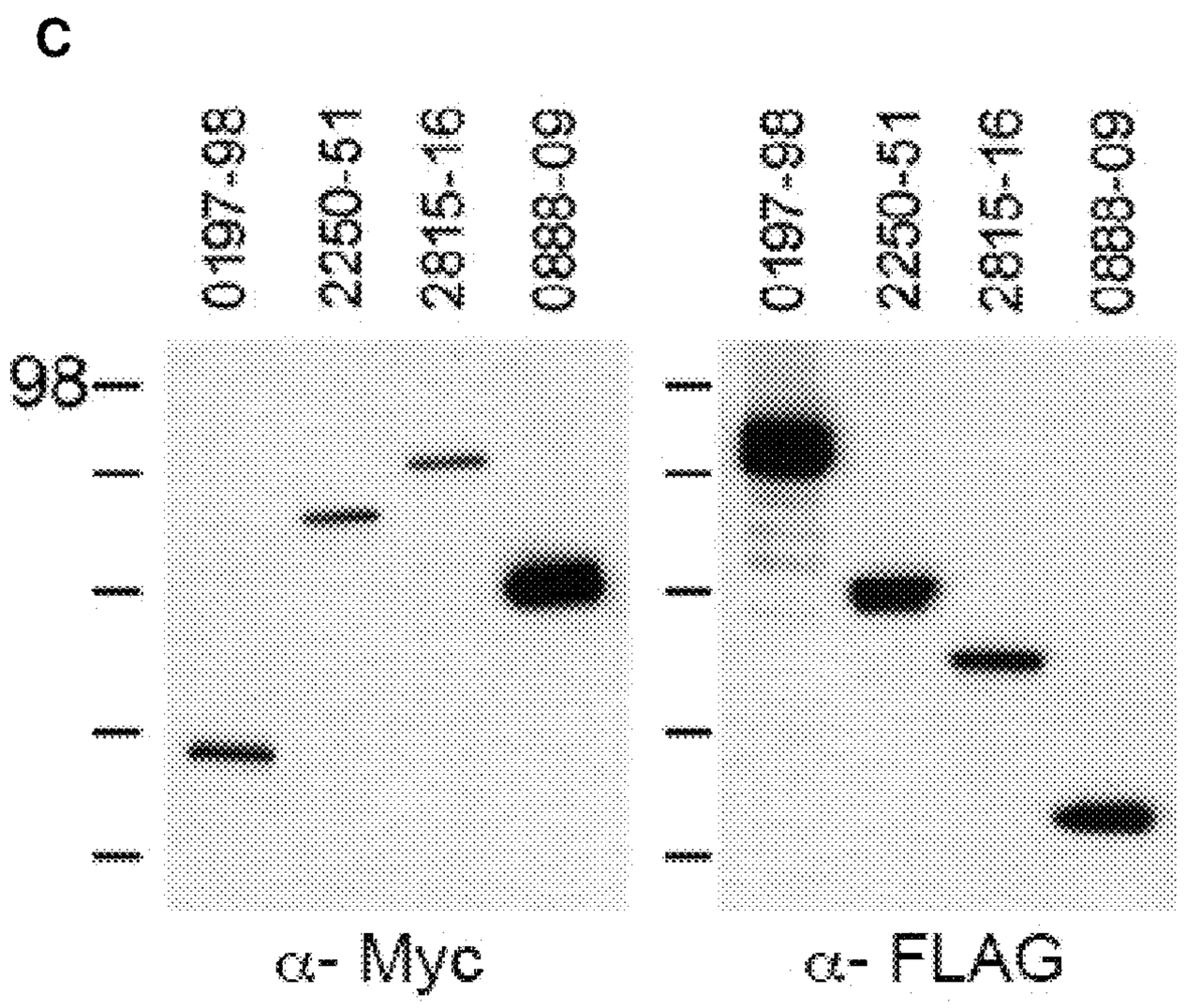

A
Promoter +Tag1
Gene 1
Gene2
Tag2
PCR
Gene 1
Gene2
Promoter + Tag1
Tag2
B
Ctrl.
888/9
Ctrl.
888/9
- + - +
- + - +
250
98
64
50
36
30
16
0888
0889
α- Myc
α- FLAG

Figure 3


C
0197-98
2250-51
2815-16
0888-09
0197-98
2250-51
2815-16
0888-09
98
α- Myc
α- FLAG

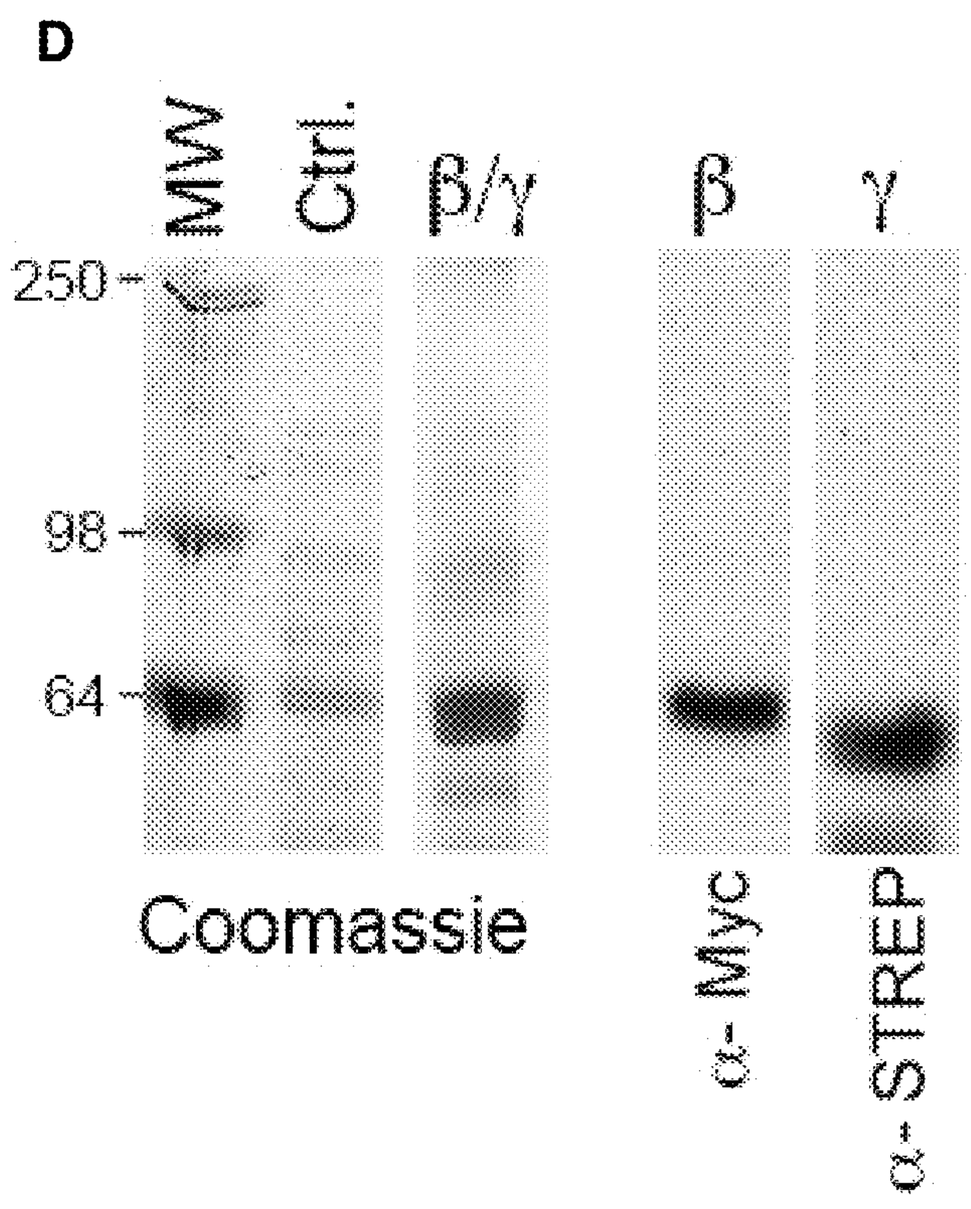

D
MW
Ctrl.
β/γ
β
γ
250
98
64
Coomassie
α- Myc
α- STREP

Figure 3

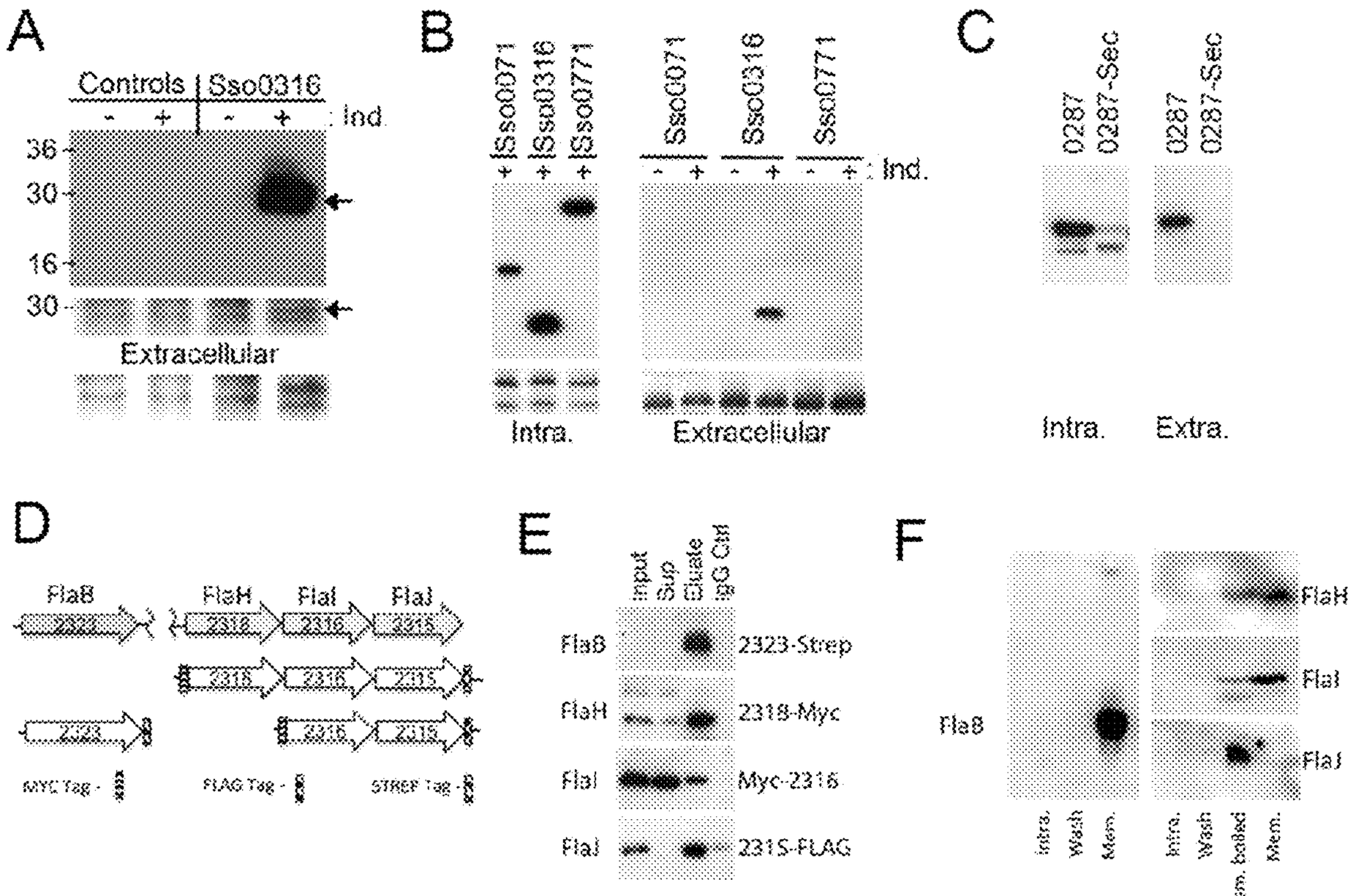

A
Controls
Sso0316
- + - +
Ind.
36
30
16
30
Extracellular
B
Sso0071
Sso0316
Sso0771
Sso0071
Sso0316
Sso0771
+ + + - + - + - + Ind.
Intra.
Extracellular
C
0287
0287-Sec
0287
0287-Sec
Intra.
Extra.
D
FlaB
FlaH
FlaI
FlaJ
2323
2318
2316
2315
2316
2315
2323
2316
2315
MYC Tag
FLAG Tag
STREP Tag
E
Input
Sup
Eluate
IgG Ctrl
FlaB
2323-Strep
FlaH
2318-Myc
FlaI
Myc-2316
FlaJ
2315-FLAG
F
FlaB
FlaH
FlaI
FlaJ
Intra.
Wash
Mem.
Intra.
Wash
Mem. babcd
Mem.

Figure 4

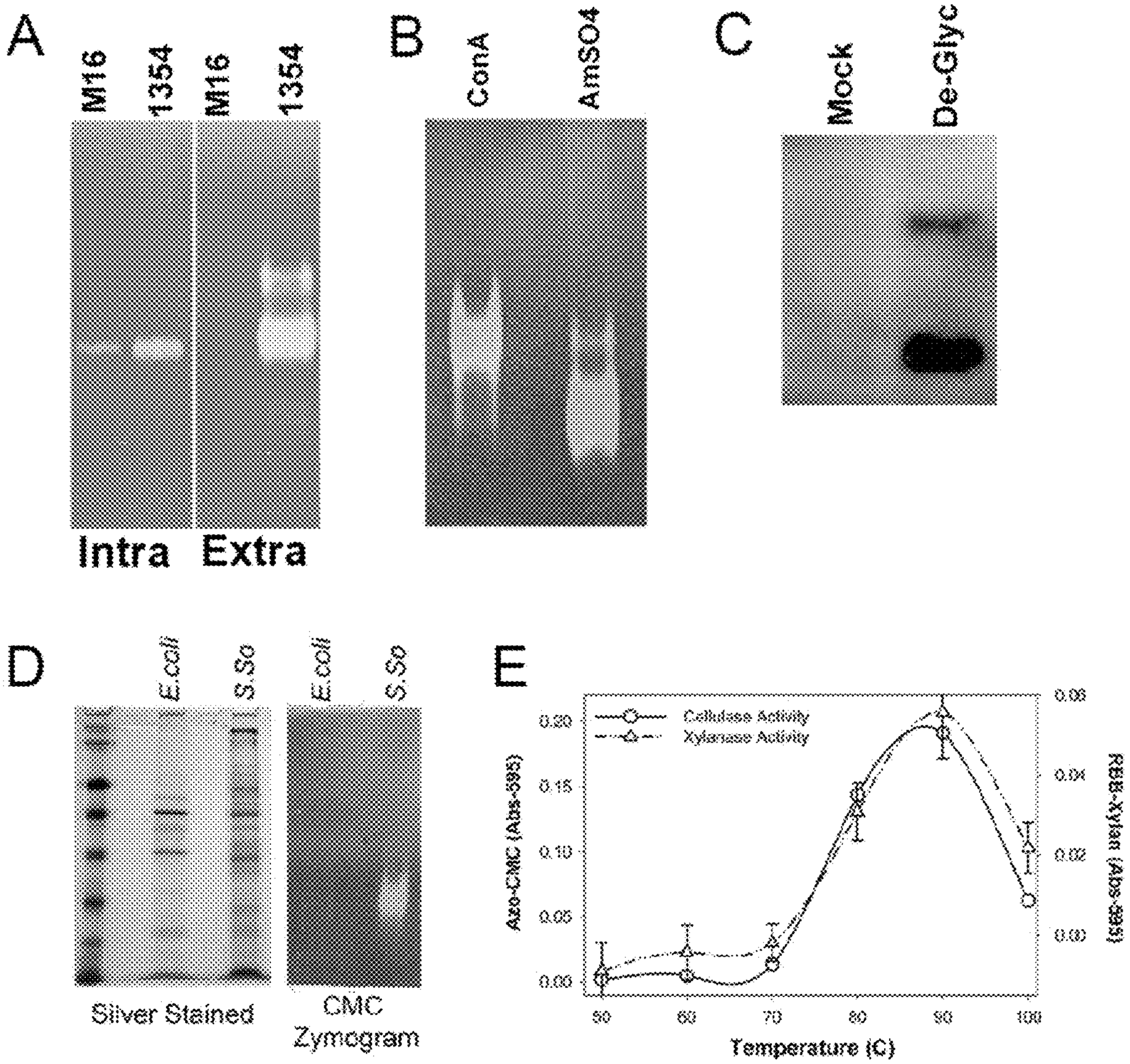

A
M16
1354
M16
1354
Intra
Extra
B
ConA
AmSO4
C
Mock
De-Glyc
D
E.coli
S.So
E.coli
S.So
Silver Stained
CMC Zymogram
E
Cellulase Activity
Xylanase Activity
Azo-CMC (Abs-595)
RBB-Xylan (Abs-595)
Temperature (C)

Figure 5

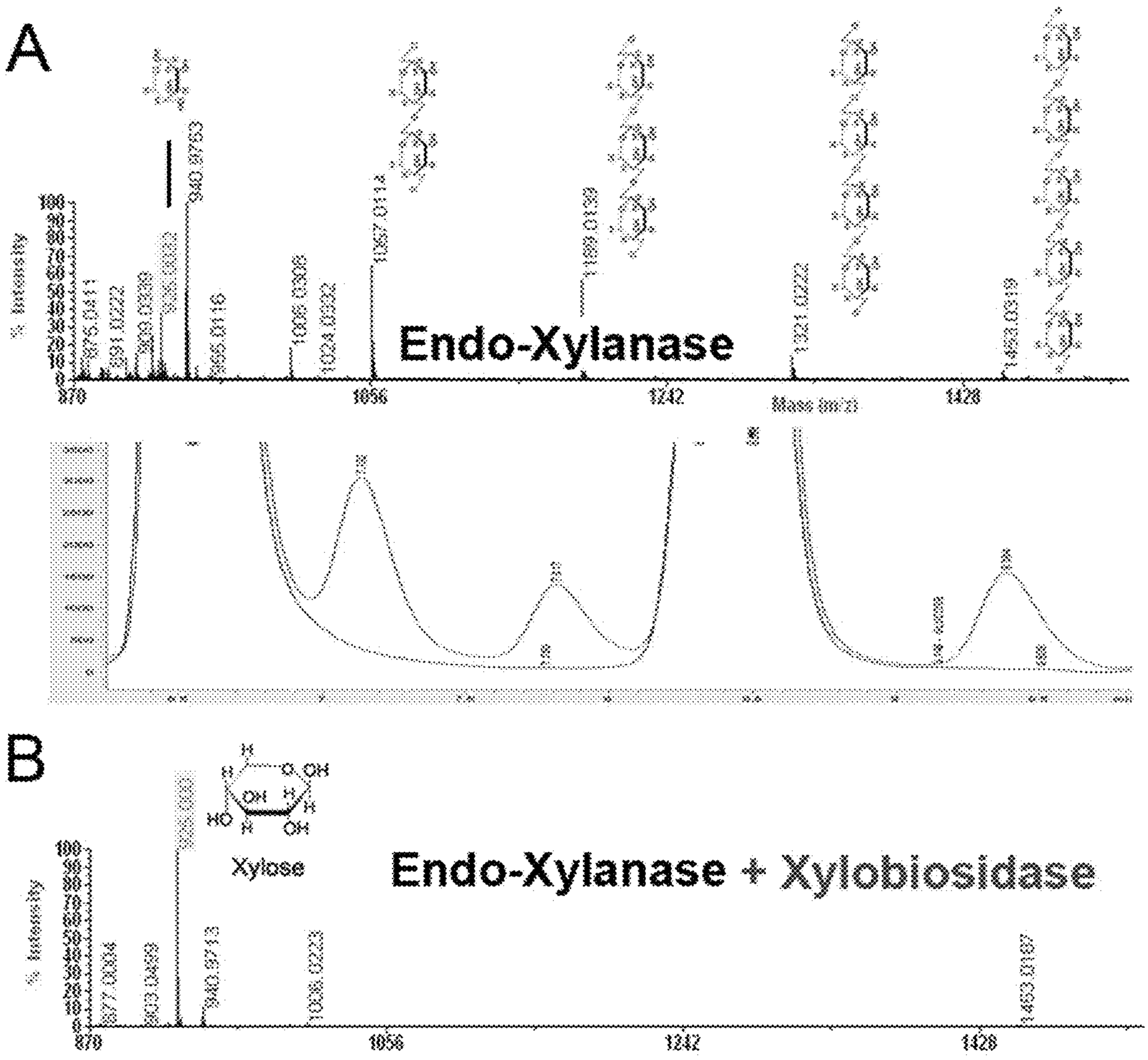


Figure 6

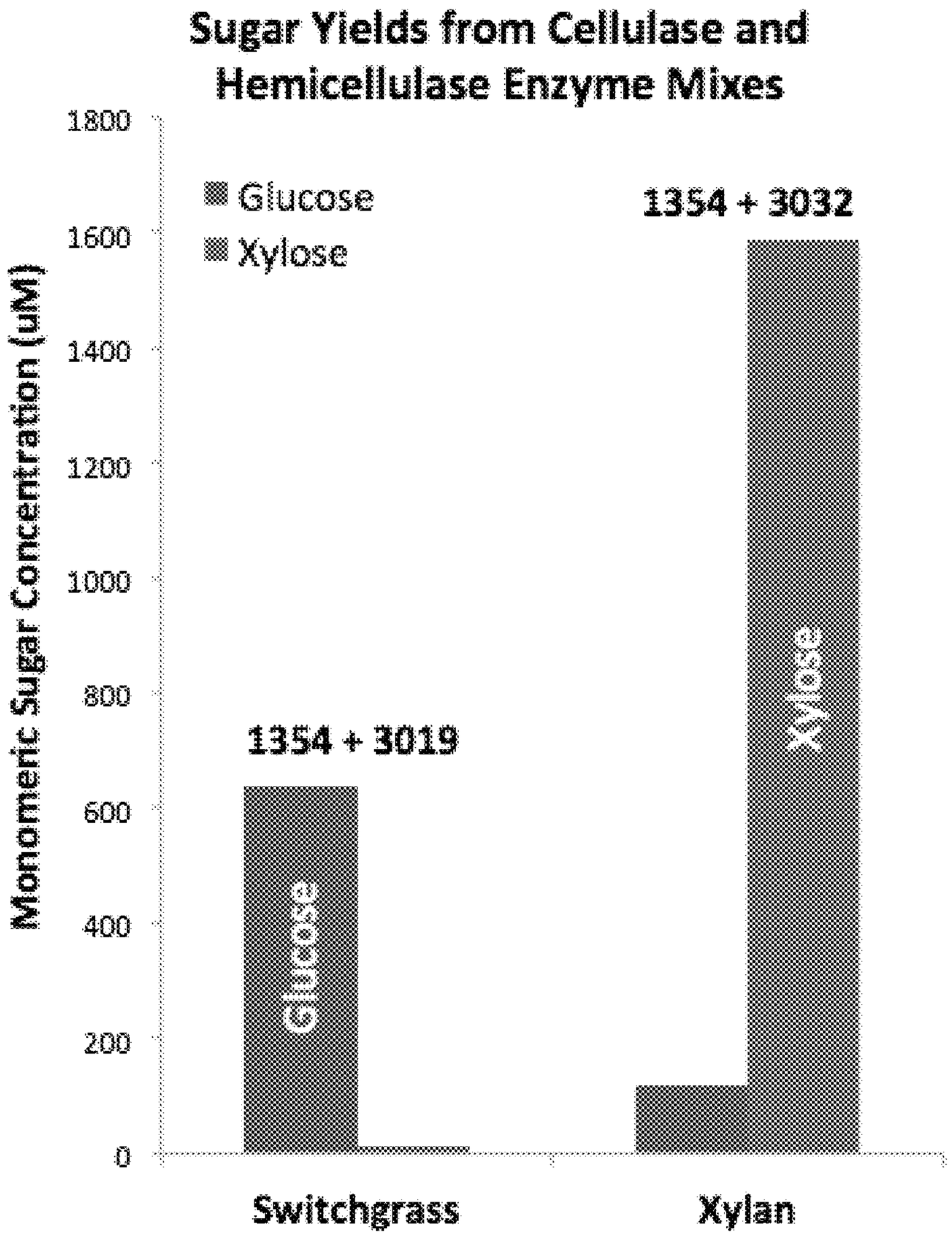

Sugar Yields from Cellulase and Hemicellulase Enzyme Mixes
Monomeric Sugar Concentration (uM)
1800
1600
1400
1200
1000
800
600
400
200
0
Glucose
Xylose
1354 + 3019
1354 + 3032
Switchgrass
Xylan

Figure 7

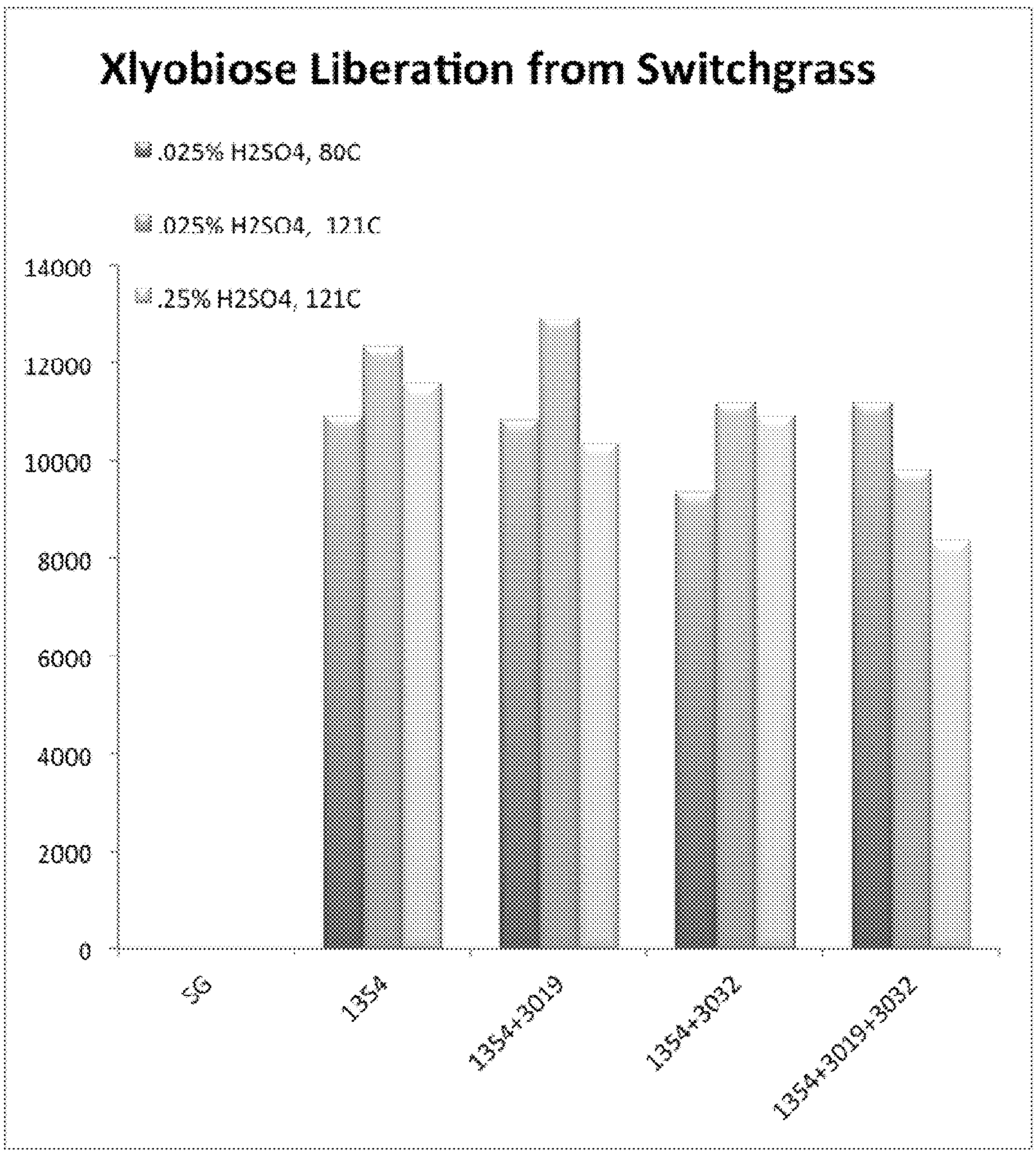

Xlyobiose Liberation from Switchgrass
.025% H2SO4, 80C
.025% H2SO4, 121C
.25% H2SO4, 121C
14000
12000
10000
8000
6000
4000
2000
0
SG
1354
1354+3019
1354+3032
1354+3019+3032

Figure 8

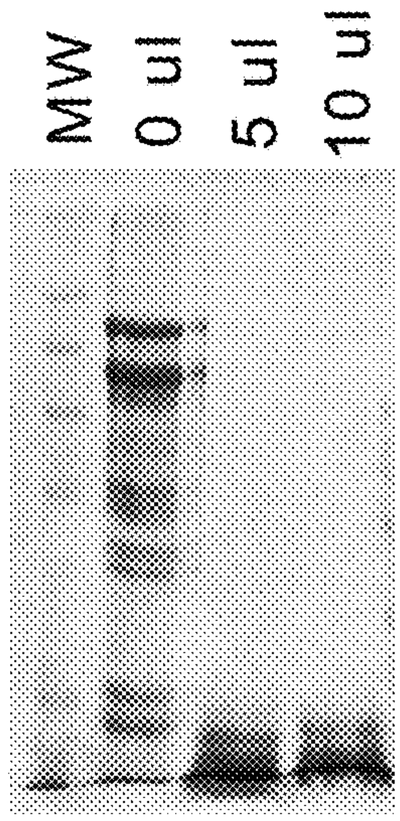


Figure 9

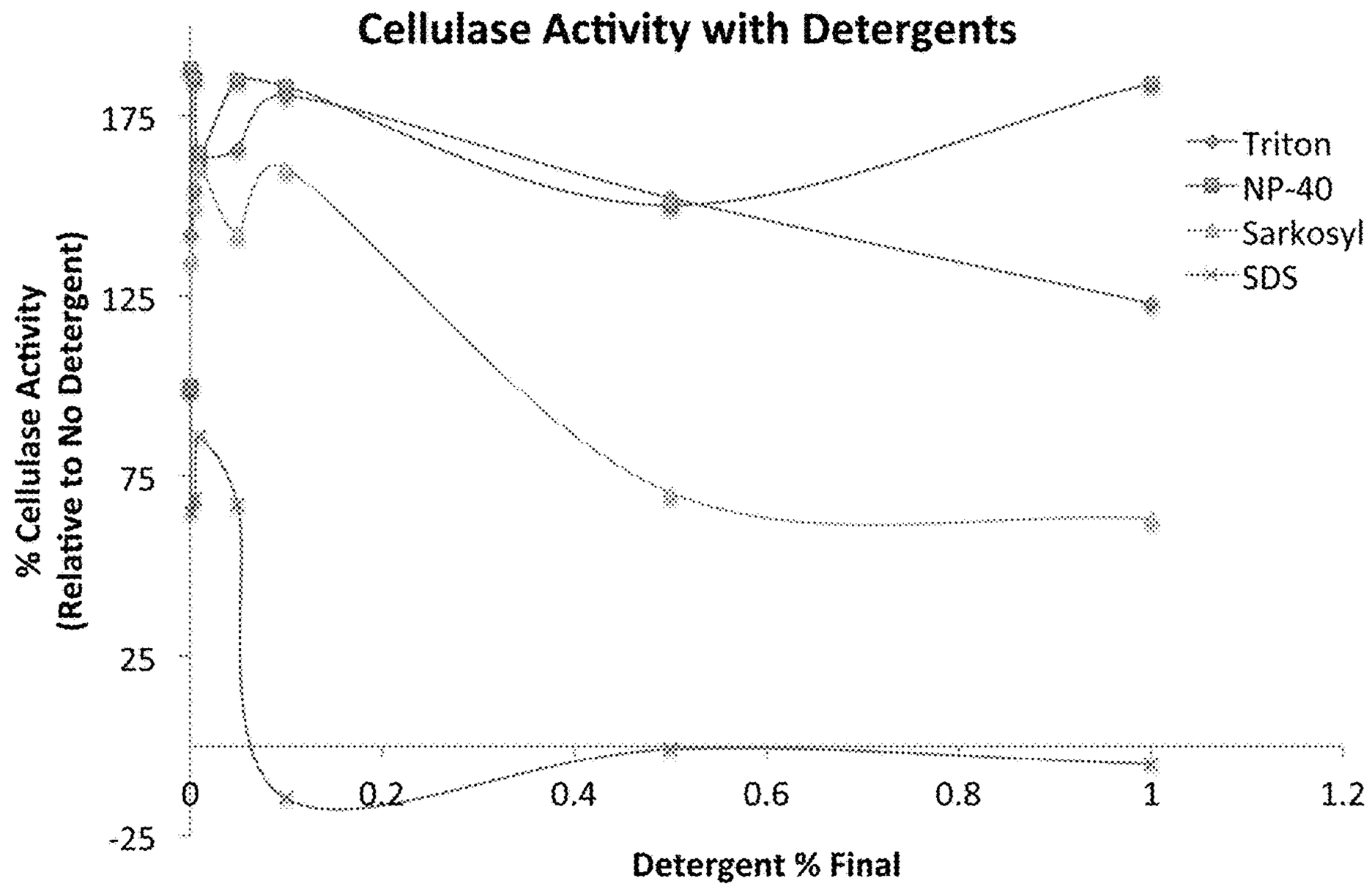


Figure 10

NUCLEIC ACIDS USEFUL FOR INTEGRATING INTO AND GENE EXPRESSION IN HYPERTHERMOPHILIC ACIDOPHILIC ARCHAEA

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. application Ser. No. 14/646,673, filed May 21, 2015, U.S. Pat. No. 10,066,223; which is a U.S. national stage entry of international Application No. PCT/US2013/071328, filed Nov. 21, 2013, which claims the benefit of U.S. Provisional Patent Application Ser. No. 61/729,268, filed Nov. 21, 2012, which applications are herein incorporated by reference in their entirety.

STATEMENT OF GOVERNMENTAL SUPPORT

The invention described and claimed herein was made utilizing funds supplied by the U.S. Department of Energy under Contract No. DE-AC02-05CH11231. The government has certain rights in this invention.

REFERENCE TO SUBMISSION OF A SEQUENCE LISTING

This application includes a Sequence Listing as a text file named "077429_1099099_SEQLIST" created Aug. 20, 2018 and containing 159,470 bytes. The material contained in this text file is incorporated by reference in its entirety for all purposes.

FIELD OF THE INVENTION

The present invention is in the field of molecular biology and enzymology for extremophiles.

BACKGROUND OF THE INVENTION

Advances in molecular biology for extremophiles have long held promise to provide a broad range of stable enzymes and novel biochemistry for industrial and bioenergy applications. Recombinant expression of hyperthermophilic proteins in *Escherichia coli* has had many successes but also proven limiting (1). Often recombinant proteins expressed in non-native organisms lack appropriate post translational modifications, binding partners, and/or fail to fold correctly, all of which can result in inactive enzymes. Broadly applicable recombinant DNA technologies for archaea have been slow to develop in part due to the highly diverse biology and environments of this domain of life (2). Many *Sulfolobus* vectors have been developed but only narrowly applied due to a number of technical challenges (reviewed in (3)). Recent advances with archaeal genetics in *Pyrococcus, Sulfolobus* and other extremophiles have reinvigorated interest in the promise of extremophilic enzymes for industrial application (4-11).

The hyperthermophilic/acidophilic microbe *Sulfolobus solfataricus* that thrives at 80° C. and a pH of 2-3 in volcanic springs across the globe and is among the most well studied archaeal hyperthermophiles (12). Many natural viral pathogens of *Sulfolobus* have been used for a number of years to advance the development of viral shuttle vectors for this extremophile (11, 13-16). However, the large sizes of these

vectors (~20 kb), among other technical difficulties, have made rapid and efficient cloning impractical to date (17).

SUMMARY OF THE INVENTION

The present invention provides for a novel recombinant or isolated nucleic acid useful for integrating into an Archaea or acidophilic hyperthermophilic eubacteria. The nucleic acid is capable of introducing a nucleic acid of interest into the Archaea. The nucleic acid encodes a nucleotide sequence that is capable of stably integrating into the chromosome of a host cell that is an Archea, and a nucleotide sequence of interest.

The present invention provides for the nucleic acid of the present invention comprising a single or multiple cloning site instead of, or in addition to, the nucleotide sequence of interest. In some embodiments, the multiple cloning site comprises two or more tandem restriction sequences or the destination sequences required for in vitro recombinational targeting of desired nucleotide sequences into the destination vectors into which one skilled in the art can introduce a nucleotide sequence of interest into the nucleic acid sequence of the shuttle vector. In some embodiments, the nucleic acid comprises a sequence to directed target integration via one or more enzymatic processes.

The present invention provides for an Archaea host cell, such as a *Sulfolobus* species, comprising the nucleic acid stably integrated into the chromosome of the host cell. The present invention provides for a host cell comprising the nucleic acid as a stably maintained in the host cell, wherein the host cell can be a non-Archaea or non-*Sulfolobus* species. One can culture the host cell in order to amplify the nucleic acid and isolate it from the host cell.

The present invention provides for a method of constructing a host cell of the present invention, comprising: (a) introducing a nucleic acid of the present invention into an Archaea host cell, and (b) integrating the nucleic acid into a chromosome of the host cell to produce the host cell of the present invention or maintaining the nucleic acid in the host cell as an extrachromosomal element.

The present invention provides for a method of expressing a peptide or protein or RNA of interest in an Archaea, comprising: (a) optionally constructing a nucleic acid of the present invention, (b) optionally introducing the nucleic acid into an Archaea host cell, (c) optionally integrating the nucleic acid into a chromosome of the host cell to produce a host cell of the present invention, (d) culturing the host cell in a suitable medium such that a peptide or protein or RNA of interest encoded in the nucleic acid is expressed, (e) optionally directing the protein of interest into a pathway for glycosylation and/or other post-translational modification that impacts functionality, and (f) optionally isolating the peptide or protein or RNA from the host cell.

The present invention provides for a method of expressing a peptide or protein or RNA of interest in an Archaea, comprising: (a) optionally introducing a nucleic acid of the present invention into an Archaea host cell, (b) optionally integrating the nucleic acid into a chromosome of the host cell, (c) culturing the host cell in a medium such that a peptide or protein of interest encoded in the nucleic acid is expressed, (d) optionally directing the peptide, protein, or protein domains determined to encode activity of interest for secretion by the microbe into the medium, (e) optionally secreting the peptide or protein of interest, or domain(s) thereof, or part thereof, comprising an amino acid sequence having an activity of interest into the medium, and (f) optionally isolating the peptide or protein of interest, or

domain(s) thereof, or part thereof, or RNA from the host cell or medium; wherein the peptide or protein of interest is a thermophilic enzyme, or enzymatically active fragment thereof, capable of catalyzing an enzymatic reaction. In some embodiments, the enzymatic reaction is an enzymatic degradation or catabolic reaction. In some embodiments, the medium comprises a biomass, such as pretreated biomass.

In some embodiments, the protein of interest is an enzyme, such as a cellulase or protease. In some embodiments, the enzyme is stable, or able to retain substantial enzymatic activity, under or in the presence of (1) a high temperature, such as at a temperature equal to or more than about 70° C., 75° C., 80° C., 85° C., or 90° C., (2) an acidic condition, such as at a pH equal to or less than about 4.0, 3.5, 3.0, 2.5, or 2.0, and/or, (3) detergent, such as equal to or more than 0.5% SDS, 1% SDS, 2% SDS, 4% SDS, 5% SDS, or 10% SDS.

The present invention provides an isolated or recombinant protease having an amino acid sequence shown in any one of SEQ ID NOs:25-35.

The present invention includes a rapid and effective means to screen for and produce industrial-scale quantities of acid/temperature stable enzymes. The time required for recombinant protein expression and purification has been reduced from months/years to days/weeks. The present invention is useful for targeting recombinant proteins for secretion into the media. In some embodiments, this advance precludes the need for engineering microbes to not consume the sugar produced during cellulosic degradation as the degradation of cellulose can be physically and/or temporally separated from microbial growth. The means to express multiple enzymes simultaneously on polycistronic vectors are developed which allow for the production of designer cocktails and microbes for specific feedstocks and processes. The present invention can be for the production of acid/heat-stable enzymes and multi-subunit enzymes. The present invention can be for the production of microbes designed to express multiple enzymes simultaneously.

The present invention has one or more of the following applications. The ability to manipulate the biology of microbes that thrive in the hot sulfuric acid permits commercial products and processes for cellulosic biomass saccharification. The merger of acid/heat pre-treatments with microbe growth, enzyme production and/or saccharification of lignocellulosic biomass. The technologies described here can be applied to accomplish: (1) production of enzymes that are active at lower pH and higher temperatures than currently available, (2) the ability to grow microbes that produce enzymes in pretreatment conditions, thereby greatly diminishing or eliminating enzyme production costs, (3) reduce the needed heat input for pretreatments by executing pretreatments in-line with enzyme production at 80° C. in dilute sulfuric acid, (4) to bring to market active enzymes evolved in the highly divergent Archaeal clade of life that have yet to be exploited for industrial or energy applications, (5) produce Archaeal hyper-stable enzymes with the archaea-appropriate post-translational modifications (including, but not limited to, glycosylation) and targeted localization to membranes, intracellular and extracellular compartments to facilitate solubility, stability and activity, unlike current approaches using fungi and bacteria microbial platforms, and (6) production of engineered strains of hyperthermophilic acidophilic microbes that thrive at 80° C. in dilute sulfuric acid (pH 1-4) and produce, modify, and secrete one or more enzymes into the surrounding media for industrial and energy applications.

The present invention can be used to produce one or more of the following: (a) hyper-stable enzyme mixes for industrial processes requiring extremes in pH, temperature, and stability in detergents (b) designer microbial strains that produce, modify, and secrete mixtures of enzymes for on-site enzyme production and industrial application, (c) degraded cellulosic material that is primarily monomeric sugars for biofuel and microbe-based production of other commodities, (d) production of integral and membrane associated thermal and acid stable enzymes and the related immobilized enzyme forms in membranes and membrane rafts, and (e) hybrid pretreatment and saccharification process for lignocellulosic breakdown into useful industrial commodities, including sugar. An inventive aspect of the peptide or protein is that it is stable in a detergent, or mixture thereof, such as Triton X-100, sodium doceyl sulfate, or the like.

BRIEF DESCRIPTION OF THE DRAWINGS

The foregoing aspects and others will be readily appreciated by the skilled artisan from the following description of illustrative embodiments when read in conjunction with the accompanying drawings.

FIG. **1** shows shuttle vectors suitable for propagation in *E. coli* and gene transfer to *Sulfolobus* and the rapid (10-day) cloning process: (Panel a) The parent shuttle vector (pMJ05) and the derivative vectors used for propagation in *E. coli* and high-throughput cloning, expression, and localization targeting of genes encoding acid/heat stable proteins, RNA's and protein domains in *Sulfolobus* species. (Panel b) A schematic diagram of the rapid PCR-based strategy for introducing genes into *Sulfolobus*.

FIG. **2** shows shows examples of minimal inducible promoters and inducible expression from these promoters in *Sulfolobus* : (Panel A) A schematic map of inducible promoters and the minimal promoter sequences (61 nucleotides) as defined by work in this invention retaining inducible characteristics and having increased expression levels. Immunoblots of equivalent amounts of protein extracts from *Sulfolobus* cells with integrated expression vectors carrying genetically modified: (Panel B) Sso0287 gene fused to sequence encoding an epitope tag (FLAG), and (Panel C) three recombinant proteins expressed from integrated *Sulfolobus* vectors likewise epitope-fused and driven by four different promoters then proteins visualized by immunoblot. This figure represents 12 separate constructs; Sso1440, Sso 0771, and Sso0071 genes driven by the indicated promoters. Note the elevated protein levels in strains with the 61-nucleotide promoters ('a' and 't') which are first described here. (Panel B) Quantitation of protein expression levels by using purified recombinant proteins and chemiluminiescent immunoblots shows a linear relationship between luminosity and protein quantity. This relationship is used to quantify protein expression levels in *Sulfolobus*.

FIG. **3** shows construction and expression of multiple genes/proteins from a single *Sulfolobus* shuttle vector construct: (Panel A) A schematic diagram of a PCR-based strategy to clone and modify multiple genes into a polycistronic construct for simultaneous expression in *Sulfolobus*. (Panel B) Immunoblots of protein extracts from *Sulfolobus* cells carrying a vector with two genes (Sso0888 and Sso0889) arranged on a polycistronic construct for co-expression showing both genes produce protein. (Panel C) Immunoblots of protein extracts from *Sulfolobus* cells carrying four different polycistronic constructs (Sso0197-98, Sso2250-51, Sso2815-16, and Sso0888-89) showing repro-

ducible polycistronic expression in *Sulfolobus*. (Panel D) Coomassie-stained SDS-PAGE gels (left) and immunoblots (right) of protein extracts from *Sulfolobus* cells carrying a vector with the genes encoding the thermosome β and γ proteins fused to epitope tags. This construct co-expresses genes that are not tandem but distil in the genome and have been built into a synthetic polycistronic construct for co-expression.

FIG. **4** shows recombinant protein secretion to the extracellular compartment and targeted localization to the membrane in *Sulfolobus*. (Panel A) Immunoblots and coomassie-blue stained SDS-PAGE gels of extracellular proteins from cultures of *Sulfolobus* with (+) or without (−) induction either carrying an empty vector (controls) or carrying a vector with Sso0316, a superoxide dismutase fused to an epitope tag. (Panel B) Intracellular and extracellular proteins from *Sulfolobus* with vectors carrying the noted genes, showing that only Sso0316 accumulates outside the cells. (Panel C) shows targeting of the intracellular protein Sso0287 to the extracellular space by inclusion of a secretion tag on the DNA construct. (Panel D) A schematic map of the epitope tagged pilin and flagellin genes from *Sulfolobus* constructed into vectors. (Panel E) Affinity purification of epitope tagged genes from *Sulfolobus* extracts showing expression. (Panel F) Localization of the recombinant genes to the cellular membranes.

FIG. **5** shows the recombinant production, secretion and glycosylation of heat and acid stable cellulase in *Sulfolobus*. (Panel A) Zymograms of intracellular and extracellular proteins from cells alone (M16) and M16-cells carrying the subjects vector expressing cellulase-1354. Yellow areas are due to cellulase activity in the gel. (Panel B) Zymogram of extracellular protein from 1354 culture either bound to glycosylation-specific resin (Concanavalin A) of precipitated with ammonium sulfate (AmSO4). (Panel C) Immunoblot of equal amounts of 1354 protein either with mock-reacted (Mock) or treated with deglycosylation enzymes (De-Glyc). (Panel D) Comparison of activity from the same cellulase gene expressed in *E. coli* or *Sulfolobus* showing the recombinant protein is not active when produced with *E. coli* but active when produced in *Sulfolobus*. (Panel E) Activity assays of *Sulfolobus*-derived enzyme on xylan and cellulose substrates showing temperature optima of approximately 90° C. for both xylan degradation and cellulose degradation.

FIG. **6** shows the results of the use of *Sulfolobus* enzyme mixtures and reaction conditions to simultaneously pre-treat and degrade hemicellulose to monomeric sugar products. Identification of specific xylan degradation products using enzymes produced in *Sulfolobus* with HPLC chromatography and mass spectrometry. (Panel A) Active degradation of raw oat-spelt xylan with *Sulfolobus* enzyme Sso1354 at 80° C. and pH 3.5. Reactions were run on HPLC Aminex-H column (lower chromatogram) to identify breakdown products after incubation for over 12 hours with Sso1354 at 80 ° C. and pH 3.5 (red trace) as compared to a parallel mock reaction lacking enzyme (blue trace). Reactions were also subjected to chemical modification with mass-tags to facilitate ionization of sugar products in mass spectrometer and analyzed (top mass chromatogram). Multiple xylan degradation products were identified by accurate mass measurements and are illustrated above the corresponding signals showing 'endo-xylanase activity of Sso1354 at 80° C. and pH 3.5 on raw xylan. (Panel B) Mass spectrometry was carried out on reactions containing enzyme mixes with Sso1354 and Sso3032. The addition of Sso3032 produced a single sugar product, namely xylan from the mixture of xylose polymers produced from Sso1354 alone starting from raw xylan. These data show the ability to degrade raw hemicellulose in a single-step pretreatment and saccharification process using recombinant enzymes from *Sulfolobus*.

FIG. **7** shows results of the use of rationally designed *Sulfolobus* enzyme mixes for specific saccharification processes of raw plant materials. Here we show monomeric sugar yields from digestion of switchgrass and oat spelt xylan with rationally selected enzyme combinations to yield desired monomeric sugars, glucose and xylose, respectively.

FIG. **8** shows xylobiose liberation from switchgrass.

FIG. **9** shows the results of 1 ug of bovine serum albumen (BSA) is incubated for 30 min at 80° C. at pH=3.0 either alone (0 ul), with 5 ul or 10 ul of extracellular protease preparation. The reactions are quenched by boiling in 2% SDS and run on SDS-PAGE and stained with coomassie brilliant blue. BSA degradation by protease activity is evident in both cases for reactions in dilute sulfuric acid at 80° C.

FIG. **10** shows that thermal and acid stable cellulase shows high degree of stability in various detergents under hot acidic conditions. Reactions are carried out at 80° C. and pH=3.0 with increasing amounts of detergents as indicated. Low detergent concentrations increased cellulase activity and activity is retained for most detergents up to and potentially beyond 1% v/v.

DETAILED DESCRIPTION OF THE INVENTION

Before the invention is described in detail, it is to be understood that, unless otherwise indicated, this invention is not limited to particular sequences, expression vectors, enzymes, host microorganisms, or processes, as such may vary. It is also to be understood that the terminology used herein is for purposes of describing particular embodiments only, and is not intended to be limiting.

As used in the specification and the appended claims, the singular forms "a," "an," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to an "expression vector" includes a single expression vector as well as a plurality of expression vectors, either the same (e.g., the same operon) or different; reference to "cell" includes a single cell as well as a plurality of cells; and the like.

In this specification and in the claims that follow, reference will be made to a number of terms that shall be defined to have the following meanings:

The terms "optional" or "optionally" as used herein mean that the subsequently described feature or structure may or may not be present, or that the subsequently described event or circumstance may or may not occur, and that the description includes instances where a particular feature or structure is present and instances where the feature or structure is absent, or instances where the event or circumstance occurs and instances where it does not.

In some embodiments, the Archaea is a hyperthermophilic Archaea. In some embodiments, the Archaea is an acidophilic Archaea. A hyperthermophilic organism is an organism capable of growth or is viable at a temperature equal to or more than about 70° C., 75° C., 80° C., 85° C., or 90° C. An acidophilic organism is an organism capable of growth or is viable at a pH equal to or less than about 4.0, 3.5, 3.0, 2.5, or 2.0. In some embodiments, a hyperthermophilic organism is an organism capable of growth or is viable at a temperature equal to 80° C. In some embodiments, an

acidophilic organism is an organism capable of growth or is viable at a pH within the range of from about 2.0 to about 3.0.

In some embodiments, the Archaea is a hyperthermophilic acidophilic Archaea. In some embodiments, the Archaea is of the kingdom Crenarchaeota. In some embodiments, the Archaea is of the phylum Crenarchaeota. In some embodiments, the Archaea is of the class Thermoprotei. In some embodiments, the Archaea is of the order Sulfolobales. In some embodiments, the Archaea is of the family Sulfolobaceae. In some embodiments, the Archaea is of the genus *Sulfolobus*.

In some embodiments, the nucleic acid encodes a nucleotide sequence that is capable of stably integrating into the chromosome of a host cell that is a *Sulfolobus* species, and a nucleotide sequence of interest. Suitable nucleotide sequences that are capable of stably integration into the chromosome of a host cell that is a *Sulfolobus* species include, but are not limited to,

CGCCGCGGCCGGGATTTGAACCCGGGT-CACGGGCTCGAGAGGCCCGCAT (SEQ ID NO: 1), TGCCGCGGCCGGGATTT-GAACCCGGGTCAgGGGCTCGAGAGGCCCGCAT (SEQ ID No:2), GGGGCGCGGACT-GAGGCTCCGCTGGCGAAGGCCTGCACGGTTCA (SEQ ID No:3), GGGGGCGGACT-GAGGCTCCGCTGGCGAAGGCCTGCACGGGTTCA (SEQ ID NO:4), and TCCGCTGGCGAAGGCCTGCACGGGTTCA (SEQ ID NO:5). In some embodiments, the nucleotide sequence that is capable of stably integrating into the chromosome of a host cell that is a *Sulfolobus* species comprises a nucleotide sequence selected from the group consisting of:

GCCGCGGCCGGGATTTGAACCCGGGT-CASGGGCTCGAGAGGCCCGCAT (SEQ ID NO:6), YGCCGCGGCCGGGATTTGAACCCGGGT-CASGGGCTCGAGAGGCCCGCAT (SEQ ID NO:7), TCCGCTGGCGAAGGCCTGCACGGGTTCA (SEQ ID NO:8), and GGGSGCGGACT-GAGGCTCCGCTGGCGAAGGCCTGCACGGGTTCA (SEQ ID NO:9), wherein is C or and S is C or G.

In some embodiments, the integration of the nucleic acid into the chromosome requires a recombinase or integrase, or a functional variant thereof.

In some embodiments, the nucleotide sequence that is capable of stably integrating into the chromosome is the integration sequence of a virus. In some embodiments, the virus is a Fusellovirus capable of infecting *Sulfolobus* species, such as any *Sulfolobus* spindle-shaped virus, such as SSV1, SSV2, SSV3, SSVL1, SSVK1, and SSVRH (see Ceballos et al., "Differential virus host-ranges of the *Fuselloviridae* of hyperthermophilic Archaea: implications for evolution in extreme environments", Front Microbiol. 3:295, 2012, which is hereby incorporated by reference). Fusellovirus is a genus of dsDNA virus that infects the species of the clade Archaea. The *Fuselloviridae* are ubiquitous in high-temperature (≥about 70° C.), acidic (pH ≤about 4) hot springs around the world. They possess a lipid membrane and a protective inner capsid in the form of a core. Exemplary nucleotide sequences include, but are not limited to, sequences for SSV1 (Accession: NC_001338.1 GI: 9625519), SSV2 (Accession: NC_005265.1 GI: 38639801), SSV4 (Accession: NC_009986.1 GI: 160688416), SSV5 (Accession: NC_011217.1 GI: 198449227), SSVK1 (Accession: NC_005361.1 GI: 42495057), and SSVRH (Accession: NC_005360.1 GI: 42494927) which are publicly available.

In some embodiments, the host cell is a hyperthermophilic acidophilic Archaea. In some embodiments, the host cell is *Sulfolobus solfataricus, Sulfolobus islandicus, Sulfolobus acidocaldarius, Sulfolobus tokodaii, Metallosphaera yellowstonensis, Metallosphaera sedula*, or *Acidianus brierleyi*.

In some embodiments, the nucleotide sequence of interest encodes a peptide or protein or RNA, of which expression in the host cell is desired, or a DNA sequence that binds a protein in the host cell. In some embodiments, the peptide, protein or RNA is heterologous to the host cell. The nucleic acid can further comprise promoters, activator sites, repressor sites, and the like, operably linked to the nucleotide sequence of interest such that the peptide or protein or RNA can be expressed in the host cell. In some embodiments, the promoters, activator sites, repressor sites, and the like can be either native or heterologous to the host cell. Depending on the promoters, activator sites, repressor sites, and the like, the expression of the peptide or protein or RNA is constitutive, modulated, or regulated as desired. Suitable promoters, activator sites, and repressor sites, include, but are limited to, those responsive to the presence of carbohydrates or otherwise regulated in response to small molecules, temperature, or other cellular stimuli. A suitable example is the AraS promoter, which is responsive to the sugar arabinose, and the Tf55 promoter which is responsive to heat shock. In some embodiments, the promoter comprises the nucleotide sequence of a Mini Promoters, such as "a" promoter, ATGTTAAACAAGTTAGGTATACTATT-TATAAAATAGT TAGGTCATAAAAG TACCCGAGAA T (SEQ ID NO:13), and "t" promoter, GCTGAGAGAA AAATTTTTATATAAGCGATACTAATGTTCTCACG-GAACGGTGTTGTGAGGT (SEQ ID NO:14).

In some embodiments, the protein or peptide, in order to be correctly folded in order to be biologically or biochemically active, i.e., possess a biological activity, such as an enzymatic activity, has to be expressed, synthesized and/or folded at a temperature equal to or more than about 70° C., 75° C., 80° C., 85° C., or 90° C. In some embodiments, the protein or peptide, in order to possess a biological activity, has to be glycosylated during or after expression, synthesis and/or folding. In some embodiments, the protein or peptide is or must be directed to the membrane, intra- or extracellular compartment for function and solubility. Where the protein or peptide has to be glysosylated, the host cell has the native or transformed means to glycosylate the protein or peptide.

In some embodiments, the promoter is operably linked to an open reading frame (ORF). In some embodiments, the ORF comprises a nucleotide sequence at the 5' end of the ORF an export or membrane localization peptide signal. In some embodiments, the export peptide signal comprises an amino acid sequence encoded by a XPO, SP, Seq1, Seq2, Seq3, Seq4, or Seq5 nucleotide sequence. The amino acid sequence of Seq4 is MKLIEMLKEITQVPGISGY-EERVREKIIEW (SEQ ID NO:22). The amino acid sequence of Seq5 is MVDWELMKKIIESPGVSGYEHL-GIRDLVVD (SEQ ID NO:23).

The XPO sequence comprises the following nucleotide sequence: ATGACTCTCCAAATTCAGTT-TAAAAAGTACGAGCTACCTCCATTACCCTACAAGA TAGATGCATTAGAACCGTATATAAGTAAAGA-TATAATTGATGTACATTATAACGG ACATCATAAA (SEQ ID NO:15). The SP sequence comprises the following nucleotide sequence:

ATGAATAAGCTGATTCCTATAT-
TTGTCGTGGTAATAATTGTACTAGGCATAATTG
TGTCTATAGAATTTGGAAAG (SEQ ID NO:16). The Seq1 sequence comprises the following nucleotide sequence:
ATGAATAAATTATATATTGTGCTTCCGGTAATTGT-
GATAATAGCCATTGGCGTTA TGGGGGGAATCATT-
TACTTGCATCAACAGTCTCTCAGC (SEQ ID NO:17). The Seq2 sequence comprises the following nucleotide sequence:
ATGAATAAAACCCTCGGTCTAATCCTAACCTCTGT-
ATTCCTACTATCCACTTTAGG CATAATAACTGGAT-
TTGTAATACCAACACAAGCT (SEQ ID NO:18). The Seq3 sequence comprises the following nucleotide sequence:
TTGGTTGTGAAAAAAACATTCGTTTTATCTACCTT-
GATATTAATTTCAGTTGTAGC GTTAGTGAGTA-
CAGCAGTTTATACATCTGGT (SEQ ID NO:19). The Seq4 sequence comprises the following nucleotide sequence:
ATGAAGCTAATTGAAATGCTAAAGGAGATAACC-
CAAGTCCCAGGGATTTCAGGG TATGAG-
GAAAGAGTTAGAGAGAAAATTATTGAATGG (SEQ ID NO:20). The Seq5 sequence comprises the following nucleotide sequence:
ATGGTAGATTGGGAACTAAT-
GAAAAAAATAATAGAATCTCCAGGAGTTTCTGGG
TATGAACACCTGGGAATTAGAGACCTTGTGGTA-
GAT (SEQ ID NO:21).

In some embodiments, the nucleic acid further comprises one or more control sequences which permit stable maintenance of the nucleic acid as a vector in a non-*Sulfolobus* host cell. In some embodiments, the control sequence is a sequence comprising an origin of replication (ori) functional in *Escherichia coli* cells. Such control sequences are capable of facilitating DNA replication in heterologous host organisms. Such control sequences can be found in plasmids such as pUC18, pBR322, pACYC184, or the like.

Exemplary vectors that are capable of stably integrating into the *Sulfolobus* chromosome include, but are not limited to, pSMY-T, pSMY1, and pSMY-A.

The nucleotide sequence of pSMY-T is:

(SEQ ID NO: 10)

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TCATTTTTTCCTAAAAATTGCTCCTTTACATTTCATCACCTTATCCTCGA
TAATCTTATTTATAGTTCTTAATGCTGTTAATGGATTCCCTGCATTATAA
ATACTTCTTCCAATGATTTCATAATCCGCTCCAGCACATACTGCATCGCC
ATAACTTCCACCTTGACTACCCATACCCGGAGAGACTATGGTCATTTTTT
CGAAGTCTCTCCTATACTGCGTTATATGATCTAATTTAGTCCCTCCAACT
ACTATTCCTTTTGGGCTTATCTCTCTTATAACGTTTTTAATATAGTCTGC
GAATAACGTACTCCATCCTTCATGTGACATTACGGCAACTAAGTATAAAT
TTTTAGAGTTTGCATCAAGATATCTTTTTAATTCATCTAGAGATCCCTTA
ACGCCTATAAAGGAATGTGCTATGAACGAGTTGGCGAAAGATAATCTTTC
AACTATGCTTTTCATTATGTATCCGATATCTGCAAGCTTAAAATCAACAA
TAATTTCCTCCACGTCTAAACCAATTAAGAGCTCTCTAGTTTTATCCACT
CCTAGATCTAAAACTAAAGGTAAACCAACTTTTATCCCATATAACTCATT
TTCCATCTCTTTAAGAACTTGATATGAGAGAGGTTTATCCATTGCTAATA
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TTACTCTACTTTTCAACATTCTTCACCAAATAATCTAGAATTGACTTCTT
TTCATTATCCTTAAGTTTATCACTCTTCAACAATTCATCTAGAATTTCTG
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GAAGCCCCTTCTTGTCTATCTATGATTACTAGTGCGTCTGAAACTTTACC
TCCACCGTTAAGAATCTCCAATGTTGCTTTCTCTATGGATACTCCTGTAG
TTGCAACGTCATCTACTAACAATACTCTTTTTCCTTTTACATCGAGTTCT
AATGTACGATTAGTTCCATGACCTTTCTTTTCTATTCTAATATATCCCAT
AGGCTCTTTAAGGTTACAAGCTATGAATGCCGATAAGGGAACTCCTCCAG
TGGCTATTCCTACTATTATATCATGGGGTATATCTTTTGCTTTCTTTATA
GCTTGATTAACTATATCGTAAAATTCTGGATAATTTGGTAAAGGTCTTAA
GTCTAAGTAATATGGACTAACCTTACCTGATGTTAAAACGAAACTTCCTA
TTAATAATAATTTCCTTTCGAGTAAGACTTCTGCGAAATTCATACGTAGA
GACTCTGCGAAAAAGAATTTAAATATACTTCTATCATAACCAGTTATAAG
GGCTTTGTGAGATTAAGACACGTAGTTTCGTCGCTTGACTTGACCAGAGA
TGACTACTTTAGAATATTCGAACTTGCAGACAAGTTCTATGATGTAAAAA
AACTAAATTATCTATCAGGGAAAGTAGTTTCATTAGCATTCTTTGAGCCA
AGTACTAGAACTGCTCAAAGCTTTCATACTGCAGCAATAAAATTAGGTGC
TGATGTGATAGGATTTGCATCCGAGGAGTCTACTTCGATAGCAAAAGGTG
AAAATTTGGCTGATACCATTAGGATGCTAAACAACTATTCAAACTGTATT
GTAATGAGACATAAGTTTGATGGGGCAGCATTATTCCctaggccGTGATT
TCGTAATATTGTAAGTTAAATTTAGCGTAGATTTTGTTTATTATATTTTT
TAGAATTTCACGAATAAAGCTTAAGTAAGAGGGATAAGCGAATAAGATCT
TGTCTTTATATACTATTATCTTTCTCGGATAAAGCTCTCTTTTAATTCTC
TTGGTTATCTCATCTTTACTGCATATTTCACATAATCTTCTTCCTCCTAC
TACGTTTATGGCATTTCTTTTGTTACATCTTTCGCACATCATATTAGAGG
AGAATGGATTTCCTATTTATTTAAAAAATTACTTCTCGGTTTAGCTGAGA
GAAAAATTTTTATATAAGCGATACTAATGTTCTCACGGAACGGTGTTGTG
AGGTACTAGTCCAGTGTGGTGGAATTCTGCAGATATCAACAAGTTTGTAC
AAAAAAGCTGAACGAGAAACGTAAAATGATATAAATATCAATATATTAAA
TTAGATTTTGCATAAAAAACAGACTACATAATACTGTAAAACACAACATA
TCCAGTCACTATGGCGGCCGCATTAGGCACCCCAGGCTTTACACTTTATG
CTTCCGGCTCGTATAATGTGTGGATTTTGAGTTAGGATCCGTCGAGATTT
TCAGGAGCTAAGGAAGCTAAAATGGAGAAAAAAATCACTGGATATACCAC
CGTTGATATATCCCAATGGCATCGTAAAGAACATTTTGAGGCATTTCAGT
CAGTTGCTCAATGTACCTATAACCAGACCGTTCAGCTGGATATTACGGCC
TTTTTAAAGACCGTAAAGAAAAATAAGCACAAGTTTTATCCGGCCTTTAT
TCACATTCTTGCCCGCCTGATGAATGCTCATCCGGAATTCCGTATGGCAA
TGAAAGACGGTGAGCTGGTGATATGGGATAGTGTTCACCCTTGTTACACC
GTTTTCCATGAGCAAACTGAAACGTTTTCATCGCTCTGGAGTGAATACCA
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ATACGCAAGGCGACAAGGTGCTGATGCCGCTGGCGATTCAGGTTCATCAT

GCCGTTTGTGATGGCTTTCCATGTCGGCAGAATGCTTAATGAATTACAAC

AGTACTGCGATGAGTGGCAGGGCGGGGCGTAAAGATCTGGATCCGGCTTA

CTAAAAGCCAGATAACAGTATGCGTATTTGCGCGCTGATTTTTGCGGTAT

AAGAATATATACTGATATGTATACCCGAAGTATGTCAAAAAGAGGTATGC

TATGAAGCAGCGTATTACAGTGACAGTTGACAGCGACAGCTATCAGTTGC

TCAAGGCATATATGATGTCAATATCTCCGGTCTGGTAAGCACAACCATGC

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CAGATAAAGTCTCCCGTGAACTTTACCCGGTGGTGCATATCGGGGATGAA

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ATTATGTAGTCTGTTTTTTATGCAAAATCTAATTTAATATATTGATATTT

ATATCATTTTACGTTTCTCGTTCAGCTTTCTTGTACAAAGTGGTTGATAT

CCAGCACAGTGGCgCCGGCCGCCACCGCGGTGGAGCTCGAATTCGTAATC

ATGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACA

CAACATACGAGCCGGAAGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAG

TGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCAGTCG

GGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAG

AGGCGGTTTGCGTATTGGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGC

TGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCG

GTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTG

AGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGG

CGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGC

TCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTT

TCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTA

CCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCAT

AGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCT

GGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCG

GTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTG

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TTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAA

CTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCG

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ACCTGACGTCTAAGAAACCATTATTATCATGACATTAACCTATAAAAATA

GGCGTATCACGAGGCCCTTTCGTCTCGCGCGTTTCGGTGATGACGGTGAA

AACCTCTGACACATGCAGCTCCCGGAGACGGTCACAGCTTGTCTGTAAGC

GGATGCCGGGAGCAGACAAGCCCGTCAGGGCGCGTCAGCGGGTGTTGGCG

GGTGTCGGGGCTGGCTTAACTATGCGGCATCAGAGCAGATTGTACTGAGA

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ACGTCAAAGTTCCCACAACAATAATTCGGGTCTTCGGACTCGTTATAGAC

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TGAAGCCTTCATCATATTCGTTCAGTACCCTAAAGCTTATACTATCAATG

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TCTATCAATCTTAATCTCGTGGATTAATGATAATAGCTCTCTGACATCCT

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TTTCACCTTAGCAAACTCATCTAACGTTGTTTGTCTCAGTTCTCTTTTCT

TTATCAAATAAAATTCCGAATGTCCCTTCTTATTGTTATTACTGTACTTC

ATGTCAGTTCACTGCTTTGCCTTTATAAATCCTTGATCCGTTTGCTCAAA

ATTTGCGGGCTGGGCATCAAATATCTTAGCTATATTGTCTTGTGTTTGCT

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TTTCTGTTTTTGTATTGTACTTCACACTCGTCTGGATGTCTTTCGCAAAT

AGCTTTCAATGCTCTCTGTATGTTATACGCACTCGGGACTGAAATCTCAA

ATTGAGCTAGTATATCCTCTAACGTTAATTCACCTTTCTTTTCAAGAATT

TTATACATTATTTCCGCCATCTTGTATGAATTTAGAGTTTGTGCCATATT

CCCATCCCACTCTATCTATACTCTATGTATAAATTAGTATTTAAGTCTTA

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TTATACAAAAAATATGGGATGTGCAAAATCTGAGCTACTAATACTGCTTG

AATATATAGATAGAGAGTGTAAGGACTACGAGAGTTGTAAAAGAATAATA

GTAGAGCTAGAAGAGAGAGTGAAGAAAATAGCTTTCGTAGAAGCAATAAA

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GATTTCCTCGGCATACGCTATCTATACTATATTAATATGATAATATTAAA

TGATTCACGATATATAGATAGAGTATAGATAGAGTAAAGTTTAAATACTT

ATATAGATAGAGTATAGATAGAGGGTTCAAAAAATGGTTTCACCCCAAAC

CCGAAAAGAAGAAGAGTTATTAGAAAAACAAAATTCAGTTTTTTATTTGT

TAACTTTAGGAAGGAAACCGTATGGTTCATATTTGCATATAAAAATTGAA

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The nucleotide sequence of pSMY1 is:

(SEQ ID NO: 11)

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The nucleotide sequence of pSMY-A is:

(SEQ ID NO: 12)

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ATCGTTAGTGGTAGGTGCCTACTCGGGTATAGCACCGCCAAGTATTCCACCGGTACCTACATATGCTTCAGCCCA

ACTCACGGCAAGTCTAATCACATGGACAGTGGGATGGCCTCCTATTACATTATGGCCTCAGATAACGCTTATTCC

GCCGTTTTCGATTTTGGGTGCAAACTTCCCCGGCTTAACCATTCCTAGCTTAACGATACCCGGTGTAACGCTCTT

CTCAATAAGCTTCAGCTGGTTAGCCCCAATTATTTATATTGCAAATTGGATCATTTGGGTCTTTCAGACTGTTGC

TAGTGTGCTATCTTATTTACTTAATATCTTTACGGGTTCGGTAGGTCTATTGAGTAGTGTACCCGTCTTAGGGCC

ATTTTTGACCGCCTTCGTGTTGATAGTTAACTTCGTGTTAGTGTGGGAATTAATCAAGTTAATTAGGGGGTCGGA

ATGACGGAGTATAACGCAAACAGTATAAGGGCTAAGATACTGAGGCGTAAAATCCTTCAACTGATTGCGGAAAAC

TACGTTTTGTCAGCGTCGTTAATCTCTCACACACTCTTACTCTCATACGCCACAGTGCTTAGGCACTTGCGTATC

-continued

CTTAACGATGAGGGCTATATCGAATTGTATAAGCAAGGTAGGACGCTATACGCAAAAATCCGCGATAATGCGAAA

CAAATTCAGATTCTGAATTCAGAACTGGAGGGGTTTAAAAACGTAAGCGGGAAGCCGATATTGACCAAGGATGAG

ACTCCTAAGGAGTTTGGCAAGAAAGATAGCCTCACTCAAAGAGGCTAAGGTTGCACTAAAAGTAGCAAGCGACCC

CAGAAAGTACTTCAACGAAGAACAGATGACTGAGGCTTACAGGATATTCTGGCAGACATGGGACGGGGACATAAT

TAGAAGTGCTAGAAGGTTCGTGGAAGTAGCAAAGGCAAACCCCAAGCTCACAAAAGGTGAAGCAACCAACATAGG

CGTATTGTTGGGCTTATTCATCTTCATACTAATAGGTATAGTACTATTGCCCGTAATCGTTAGCCAAGTCAACAA

CCTCACAAGCGGTACTTCACCCCAAGTAACCGGTACTAACGCCACACTCCTGAACTTAGTGCCGTTATTCTATAT

CCTAGTCCTCATAATAGTCCCCGCAGTCGTGGCGTATAAGATATACAAAGACTGAGGTGTGAGGGATGGAAATCA

GTTTAAAGCCAATCATTTTTTTGGTCGTTTTTATCATCGTAGGGATAGCACTATTCGGCCCTATAAACAGTGTTG

TAAATAACGTTACCACATCGGGAACCTACACTACTATAGTTTCCGGTACTGTTACTACGTCTTCATTTGTGTCAA

ATCCGCAATACGTAGGTAGCAATAACGCTACTATCGTAGCCTTAGTGCCGTTATTCTATATCCTAGTCCTCATAA

TAGTCCCCGCAGTCGTGGCGTATAAGTTGTATAAGGAGGAGTGATATGAAGTGGGTGCAAAAGGCGATAAAGAGA

CCCGGGAGGGTACATCGCTACCTTATGAGGCTCTACGGCAAACGGGCGTTTACAAAAGACGGTGACATAAAGGCA

AGTTATCTCGATAAGGCGATAAAGCACGTTAAAAAAGCTAAGATCCCGAAAGAGAAGAAACGTAGTTTACTGTCA

GCCCTACTGTTAGCGAAAAGGCTTAAGCGGATGCACCGCAAGTAGGCCCTTTATAAAGTCATATTCTTTTTCTTT

CCCTGATGAGTGCGTTAGGGGATGTAATCTACATCTTGGGTTTTCTCTTTCCGGCTTTAGGGCTAATCAGCCGAA

ACTATCTTGTTAACTTAATGGCATTCATAATAGGAACAGTCGCCTTTTTGGTCTTCGTCCAAGGCTATACCGATA

TAGCGTTCAGCAGTTCGACGTTTTACTTAGGAGTACTGCCTCTACTACTTGGTCTCGTCAACTTAGGCTATTTCT

TCAATTGGTTGAGGGAGGAAAGGATATGAGGTGGGGTAGAAGAGATGATAGGGATACCGGCAAAATACTTCGAAA

TAGGAGTCGTAATAGATTCAACATTTATCATTATGTCTCTACTGTTAAGAAAGTCAAAGAGACAGAGAGAGAACT

CCTTCGACTTACGCAAACATGGAAGGCTATTAGGCTTATATCTTATAATAGCGTCGGCATCAGCATTAATCGTCT

CACATCTCGCCTTATACACAAACTACATGAACTACTTAACGGGCTTATCTCTTAATGCGTTTCTGTTTTATCTTG

GGTTGAGGTGTTTGCATGTCTGATGGGAAACTCCTTTCTGCTTTCGAGGAGGAATTAAGAAAAGCCCAAAGCCTA

GAGGAATTAAAGCAAAAGTATGAGGAAGCCCAAAAACAAATAGCTGACGGCAAAGTACTAAAGAGGCTATACAAG

GTTTATGAGAAAAGGCAAACAGAATTAATGCTTCAGCAATATAGGCAGATAAAGGCTGAACTGGAAAAGAGGAAA

AAGGTAAAGAAAAAGGATAAAGCCGACATAAGGGTTAGAGTAGTAAAGAAGTGGATAAATTCACGCTTATTCAGT

GCTGAGCATTACGTCGCATTACTGCAAGAAAATCAAGACGGCTTATCGATACTATTTCTAAGAAGAGCAAAACTT

ATAGAAAATCAAGGCTATCTAATGCTAGAAGTGAAGAAGTTAAGGAAGGCATGGGTTTTAACGGCTGAACCTATA

CTCCTTGAAAGGTTAAAATTCCCATTCGGCAAAAAGTTTGTAGCCGTGCATTTCGTTTTACCCAATTATCCTTAC

ACACTTCAGCTTAAACCGGATGAAAAACTGAAAGAGTTAGCAGTTAAGGCGATAAACGGGCCTCAAATAATGAGC

GCAATGATACGTACAAAGTTCTTCGAAGCGTTAGCTAGGGTAGGAAGCGGGCCTGATCTGATGATGCTCATAATC

GGCGTTGTCATGGGGATTGGCATAGGCGTAGCGATAGGTTTCGGTATAGCTAACGCAAACTTAACGCATTTGCTA

TCTCAACACGTTACGAACACTACAGTGACACATACTACGACCACAACGACTTCACCCTCATTCACGATTCCCTCA

AACTCCTCAAAAGGGGTGAGCTAAAATGGTCTCAGTAACAGAAATAATAACATATGGACGAGAAGCAATAGAAAG

AATAATATGCAAATATTTTAAAGATTCGAAAATAGAAAAGATATTATTCTTGCCGAGTGAGGAAGACGTAAAGGC

AAAATATATCATTGGACGGGTAGGGTTTATAAGGATTAGTAATACGTGGTCTGGAATTGTCGTAGTTGACGGGGT

ACAAATACCTTTCGTTGCTGAAGTCCACCTTAATGGCAAGATTGATATTTACCTTTATCCTCAAAAGGACTTCTA

CTTAGCACATTTGGTGGGTGAGCTGAATGGCTAAAAAGAACGGCTTAACAGAACTAGAGCAATTAAAGAAAGAGA

ACGAAGAGTTGAGAAAGAAGTTAGAAGAGTTAGAGGCGTTGATCAATAACGATAGCGATGACGACGAAGAGTTGC

AGGAAATCGAAAACCCGTACACCGTTACAAACCGTGCAATAGATGAATTAGTAAGCCCAAAGGACACAATGTTCT

-continued

ATTTGTCGGGAAACCAGATATCGTTAATCTTAAGTGCTTTTGAATTCGCCCGCTTACCGACGTACTTCGGTGAGG

AACCGGTAACGGAGTTAGCGGAATACGCCCATAAGTTGAAACATTATCTCGTTTCGAAAGGAGGAAGAGGAAGGA

GGGATATACTGAGAGTCCTACGCGTTAGTTCAGGTCAGACAAGAGAGAACGTAAACAAATCAATTCTGAAACAAT

TATTTGACCATGGTAAGGAACATGAAGATGAAGAAGAGTAATGAATGGTTATGGTTAGGGACTAAAATTATAAAC

GCCCATAAGACTAACGGCTTTGAAAGTGCGATTATTTTCGGGAAACAAGGTACGGGAAAGACTACTTACGCCCTT

AAGGTGGCAAAAGAAGTTTACCAGAGATTAGGACATGAACCGGACAAGGCATGGGAACTGGCCCTTGACTCTTTA

TTCTTTGAGCTTAAAGATGCATTGAGGATAATGAAAATATTCAGGCAAAATGATAGGACAATACCAATAATAATT

TTCGACGATGCTGGGATATGGCTTCAAAAATATTTATGGTATAAGGAAGAGATGATAAAGTTTTACCGTATATAT

AACATTATTAGGAATATAGTAAGCGGGGTGATCTTCACTACCCCTTCCCCTAACGATATAGCGTTTTATGTGAGG

GAAAAGGGGTGGAAGCTGATAATGATAACGAGAAACGGAAGACAACCTGACGGTACGCCAAAGGCAGTAGCTAAA

ATAGCGGTGAATAAGATAACGATTATAAAAGGAAAAATAACAAATAAGATGAAATGGAGGACAGTAGACGATTAT

ACGGTCAAGCTTCCGGATTGGGTATATAAAGAATATGTGGAAAGAAGAAAGGTTTATGAGGAAAAATTGTTGGAG

GAGTTGGATGAGGTTTTAGATAGTGATAACAAAACGGAAAACCCGTCAAACCCATCACTACTAACGAAAATTGAC

GACGTAACAAGATAGTGATACGGGTAATGTCAGACCCCTTTTAGCCATTCCGCATACTTTTTATATTGCTCTTTC

GCTATGCCGAAGAGCGATACGTAATGTTGCGTTAAAACGCGTGTCGGTTTACGCCCTTGAATAAAATCGATAATA

TCTAACGGTACGCTTAGCTCAGCCATCTTAGACGCTACGAATTTGCGGAAGTACTTTATCGCTATAGCGTCCTTA

TGACGTCGTTCAAAGTCCGCTATTGCCCACTTCGTCACCTCTACTCTCTTCAGAGGCGTTATGTGGAATACATAG

AAGACGCCCTTATATCCCCTAGTCCAACTAAGCGGATAATAACAGACGTCGTTACCGCAAATGTCCCTTTCGGGT

TCCTTCAGCACTTTCAGTATTTCGCTCAGCCTAACGCCCGACTCGAGAGCGATACGGTAGATGAAGTAGACGTTT

TCGCTATAGTCTTTTGCTAATTGTAACGTCCTTTTTATCTCTTCCAACGTTGGAATGTAGATATCAGCGTTCGCC

TTCTTCACCTTTACCGCTTTCAATATTTTATCCGCAAATTCATCATGTATGATATTGCGTGACGCTAAGAAACGT

GCAAAGAGTCGGTAAGCCTTCTGTGCGTCTCTCGTCTCTTTATACGGCTTTGATATAGCATTGATGTAGTCCTTT

GCAGTTTTTTCGCTTATCCCCCTTTCGTTCATGAGATAGTCGTAGAACGCCTTTATGTTGCCGTCCGTCGCGTAT

TGGCGCAAATTGGCAACCAACGCTATTTTACGTCGTTCAGTTCCCTCTTTTCCGCCTCCGGAGCCGGAGGTCCCG

GGTTCAAATCCCGGCGGGTCCGCTTGTAGGGGAGTATCCCCTACGACCCCTAATTTCATTTTTAGATATGATTCA

ACGACGTCAGCTAAAGGACCCACGTAACGCTCTTTTACCTCACCGTTTTCATACTCTAGCTTGTAAACATAATAC

CGCCCTTTCCTCTCGCGTAAAATATAATCCCCGTATTTATAACGCGTCTTATCTTTCGTCATTTCGCCTCACAGT

ATTATGGTTGCCAAAACGGGCTTATAAGCATTGGCAACCCGTTAATTTTTGCCGTTAAAACACGTTGAATTGAAA

GAAGACGGCAAAGAATCCACACAGGTAATACTAAAAAAGTAGTATTACTTACATTAGAAGGACTCATTTGTCCAC

CTTGTATTCTAGCCATGCTATCTCTGCCTTCAGCTCATCTAGCTTCCCCTTTATGTCTGTCAGGTCAAGGGGAAC

TCCTCTCATTAACCTGAGTTCGTTTTCGATTTTTTCAAGCTCCTTTTCCAACTCCTCTAGTTTCTCTAATTCCTT

TAGTCGTTCTTCCAATTTCTTTTCCAATTTCCCCTTTGCGTCATTTATAATTATGCTTACTACCCAAACAATTCC

TAAATCAGAAATAATTATTAACTCCTCTGAGTTGAATATCATTTTCCGCCCCTCGCTAAATACTCCTTAAAGCTC

TGATAGAACCCCTTCAGACTAACCCGTAAGTCTGTTAGGTTCTTCCAGTATTGTAATGGGATTAAGTAATAGTAG

CTTACTGCATCTCTCTCAAATTTGTCCTTCTTAATCTTTCCTTGCTTTTCTAAGTTGAGTATTTGCAGTGCTGAG

ATACATTTTAACTTGTCCTCAGCATCTGAATAGTGTATAAACCAAACCCTCCCCATAACCTCATTCTGCTTTGCA

ACTTCTACTTTAGTGCTTAATATTGCGTAAACGCTTTCGCCGTATCTTTCTTTGCTCTGTTCTTCAGTCCATGAA

CTTCCCGTAATATCTATCCAAATTAAAGGATAATATTCTGTCTTAGCCTTAACGTATAAAGTCAAATCGTATTTA

TCTTGCAGACCGCTATAGTATTGCTCATTTATTACATTAGTTAAAGTCCCCACGCCAGTTGGGCGGATATAAACA

TCAAAGTCTAACAAACCCTTAGCCCGCCACTTTGATAAAGAGATTAAGAGCTTTCCAAAAACTAGGTATTCTCGC

CCTAAATAAGTTGAAGGGAGGATATAATCCTCAGCTTGATTACCCCAATACTTTAGCTTAAAATTAGTTTCAGCC

-continued

ATCTCACTCACCATATTGAAACGTGGGCTAGTATGTGAATCAGTACTGATGCTATTGCAAATAACACACTTGCAG

TAGCAATTCCTATTACAATCCATTTACCATAATCCACCTTAGTTTGTTGGTCAATATACTCGTTGATGATCTTTA

GTATTTCTGGCTTTAGTTCTGATAATGAAAGGAAGACAGAGGCATAAAGTACTAAGGAGGATGTGAACAGATTAT

CCGCCTTTTCTGAAAGTTTATAAAGCTCATATCTTGCTCTCTCATAATCTTCATAATTAATAATTTCATCAAACT

TTTCTACTTGCTCTTCATATTCTTTCTTCAGAGAGTAAGGAGTTGTCTTTTCAATTACTCCTAATTTTATTAACT

TCTTAACAGCTTCCTTAAATCCTTGTTTATTGCTAGCATACGCTAAAGGGTCTTTTCCTTCTTGAGAAGCTCTAT

AGATAACTATAGCACCATAAACAATATTTACAATATCGTATGGTAAGGAATACGCACCGATTTGGGCAATATCTT

CAACTCTTCTTTGATCCATCTAGTTCACCTCTTTTTGATTTGTTTGTAGGTTTCTATCGCAGTTTTCAGCGATAT

CGCAAATAGCTTCCCCTTTTCCGTTAGGTATAGCCTCTTTTCGCCTCTTTCTTGACGCTCTTTCACGAAGCCCTC

TTGTATTAGGAACTTTTTTGCATCATAAAAGGTGGCAGTGGACATGGGAAATTCTGCGTTTACTTTCTTGTATAG

GTCATATGTTGCTATTCCTTCATTATCATATAGATAAGCCAATACTATGGCTTCGGGGTAGAAGAATGGTGTACT

TTTCATATCCTCCTCACTCCTCAGCCTCTAATAGCTTAACTGCCTCCTCTATCAACTGTCCCATTGTCTTTCCAG

TCTTTGCCTTAAGCCTCTGCAGTAAATGGTAAAAAGATTTTACTTATTCCGTTCTCTTCTGAGAACCGCTTGCTT

TTTACGATTAAATTCCACATATCATCTAAGATAGAGTGTTGTGGTTCTAGCTTCCTCGTGTAGATTTTCCCCTAT

TAATGTTAGTTTATAAAGACCGGCTATTTTTTCACTAATT

In some embodiments, the suitable medium comprises plant cell wall, or one or more component thereof, as a carbon source. In some embodiments, the components are cellulose and/or hemicellulose. In some embodiments, the components are xylan, glucuronoxylan, arabinoxylan, and/or xyloglucan. In some embodiments, the components are glucose, xylose, mannose, galactose, rhamnose, and/or arabinose. In some embodiments, the suitable medium comprises plant cell wall, or one or more components thereof, as essentially the sole carbon source. In some embodiments, when the suitable medium comprises a plant cell wall, or one or more component thereof, as a carbon source, the peptide or protein of interest encoded in the nucleic acid stable integrated into the host cell chromosome is a cellulase, or an enzyme for digesting the plant cell wall, or one or more component thereof, or a functional variant thereof, or a enzymatically active fragment thereof. In some embodiments, the peptide or protein of interest encoded in the nucleic acid stable integrated into the host cell chromosome is a thermostable or thermophilic enzyme or protein. In some embodiments, the peptide or protein of interest is enzymatically active at a temperature of equal to or more than about 70° C., 75° C., 80° C., 85° C., or 90° C. In some embodiments, the peptide or protein of interest is enzymatically active at a pH of equal to or less than about 4.0, 3.5, 3.0, 2.5, or 2.0.

Such enzymes include, but are not limited to, enzymes with the following enzymatic activities: glycoside hydrolase, cellulase, xylanase, endoglucanase, cellobiohydrolase (CBH), and β-glucosidase (BG). Suitable examples of such enzymes include, but are not limited to, those described in "Thermophiles biology and technology at high temperatures," F. Robb, G. Antranikian, D. Grogan, and A. Driessen, CRC Press 2007, which is hereby incorporated by reference. Other suitable examples of such enzymes include, but are not limited to, those described in U.S. Patent Application Ser. Nos. 61/172,653 ; 61/172,668; 61/246,439; Ser. Nos. 12/892,724; and 13/265,786; PCT International Patent Application No. PCT/US2010/032320; and, Park J I, Steen E J, Burd H, Evans S S, Redding-Johnson A M, et al. (2012) A Thermophilic Ionic Liquid-Tolerant Cellulase Cocktail for the Production of Cellulosic Biofuels. PLoS ONE 7(5): e37010. doi:10.1371/journal.pone.0037010; which are hereby incorporated by reference.

Other suitable enzymes include enzymes having a protease activity, such as a protease. Exemplary proteases include, but are limited to, the following:

An exemplary protease is Sso2551 comprising the amino acid sequence as follows:

(SEQ ID NO: 25)

MESRIIQVVVISTFLVLSVLFPLLSLAYSTTSINPSYPQSNVISALPSNT

NIILYFFIPPKNLNELYLIAQEVANHQIKPLSNAQLVSMFSNQDKVNESI

KYLESKGFTIIYRSPFEIMAEAPVSLVSSVFETSFVLAKSTNGEIYYKPA

GNVKIPSTLNNLLIGGLTNFTNVSLPLIQLGKLENGNLIPNKQAYSSFVY

TFQFSATWYTPKVIEGAYNITPLLNSTADKKVTIAIIDAYGDPEIYQDVN

LFDARFGLPPINLTVLPVGPYHPENGLFTGWFEEVALDVEAAHAAAPYSN

ILLVVAPSATLEGLFSAIDVVVSEDLAQVVSMSWGLPGILFGASGFYAVF

NGIIFPNYPYYDYYFELGSAEGITFLASSGDLGAYNDLPTVYGSANYPAS

SPFVTAVGGTSLFANITSGYISTYNSTGNFGAEIAWSVNPLYFGVIQGGV

SSGGGYSQLFPAPWYQRYVTHSNYRAIPDVAADANPYTGFTIYALGQEVV

IGGTSLSAPLWAGIIADIDGIIGHPLGLVNPILYEIYQNTTLYHQAFHQI

SLGYNGYYYANSSYNLVTGLGSPNAGMLGVIIKHSLSKSLAISVSTFETG

VFQPWYFYGSTFTIAAYITYPNNTIVSQGSFNAYIYTSEGYLATVPLSFN

GSYWVGNYTITPNNPPNLWEIVVNGSSDQFTGVGTVEVDVGESININSPI

PYPYSFPIPYNSPFGIEAWIYYPNGTPVVNQSVTAYLVSNDGKLLASIPL

TMMAPGLYEGSYALLPPLPQGTYLLIVNDSYGSAFSYVYFGEYNFGAILT

PINDGFPAASPGQNITIIDEVLTPELTGLFTSNVTAYIYNQHGNLIDQVK

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LTPAPDEIQFGVYLLFFLYYANFTIPFDASPGFYNVVIQSISNTSTGLVK
ADFITSFYVSPANLTLNVKVNNVVYEGELLKIFANITYPNGTPVKYGMFT
ATILPTSLNYEQLIIGFEAGIPLQYNSTLGEWVGIYSIPSIFYGSIFQGS
SVYSLAGPWNVIVSGVSWNGYNLYSTPSSFNFVNVMPYTFINNIVVSSKS
LDSPLLSKINSTTYMLSNVKSNNITINGMNVILSNVIANTVTVKNSNIMI
TSSTINQLVLDNSSVSIIGSKIGGDNIAVVANDSNVTIVSSVIQDSKYAF
LQPNSVISLSGVNMYNVTSLSSIPAPRITYLSTTNVTTSKESIIVNITGE
YLRLLGVSMNNKPVGYSVISSSPSSISLSIPFNASQLSDGQYIFTVSISD
GLPYNLTFNLLNNYHLIIVQDHLKALQGSVNLLTVIAIISLIIAIIAVAL
LFVFTRRR

An exemplary protease is Sso2045 (Cannio et al., *Protein Pept Lett.* 2010 Jan.; 17(1):78-85) comprising the amino acid sequence as follows:

(SEQ ID NO: 26)
MRLLKILLLAMLILPLFSFFTLSISLYDQIQLPPHYLFYISENATQGSGI
DVIFYTSSPITFMIMTPSQFYQFNQTGSSQSIYSITTNSLSKFFPLSGQY
YIVFYNNISNNPVTLNYYILTRPLPTGIADYGLKINNGVISPYIEKIKSV
IGAVEINKLLAYNSTPPAGVSQYSASIQLNVVLQVNTIGGSQQLWLQNVI
QIYTNNDSYIFLDNIWNFTGKISILSNSTVKGNGIVYVTNNGNDYYAYGT
NFSTLLIPSLKYLLINTSYTSQGPMISFGYMNQSGSPIWYDNVTILIPNT
LSAYILVDGYNFTAGGLAYDAELILGGGGNGEFTFFNESNVELAMIYQYL
NGTLAPPKFLFPFGLDTEESADNLYSISYNGVYLVSSGYQVINNLNENVS
QLRFNVVNYTKATDQNFPYIFTINVSGGVLPYKLNVTISNSSGNELSGYT
YVLFPSVSTYYLFLSPLSPGNYTVKIKLTDFNGNSKSYEFSLTINPPLKV
QILNVTNYIDLALPYFNFTSIISGGTKPYNIIITISNDSGILSETYKIIN
YTSITYYAVNMKGYSIGKYTIQIEVEDYAGSINISKYNFTINPNPYISTL
SYTSETDKGLREVIKAIGKGGSGSLIYYWYVNNSLVSSGIGDELYNFTPS
NIGEYNITVMVKDVLGVSSAKSVIIKVNPDPVVELSVPKTTIDSGAEFPV
NATVSLGTPPYYISWYINGSYVGNESIKELNLSSIGVYIITVTVRDSAGY
IINMSKPVLIVPPPSLSVKEQTQGNFIQYNTSIALSASVNGGTDPYYLIF
LNGKLVGNYSSTTQLQFKLQNGENNITLIAKDLWGKTAVKTLIVNSGYNY
VGIGIIAGIILIIVIVVILVISKRK

An exemplary protease is Sso2088 comprising the amino acid sequence as follows:

(SEQ ID NO: 27)
MESKNVILKRVMLLLVLILSTTTFLTIIAQSQAQYYYIQTSSPQYTIIPG
SVFVEPLNSSQTLYIAVLLNFTNLASLQSYLNEIYLSAPQFHHWLTPSQF
REYYYPSRSYVNSLIKYLESYNLQFLGNYGLILVFSGTVGNIEKAFNTYI
NVYYYPFKNLYWFGLLGIKNIGPFYYYSNNVTPSLPFNIGKYVLGVVGID
SLDPKVVNVVTQTWHLPMVKAQSGLVSKAIISPITIEQYFNFTLAYERGY
TGGGSNIAIEGVPESFVNVSDIYSFWQLYGIPRTGHLNVIYFGNVTTGGQ
SGENELDAEWSGAFAPAANVTIVFSNGYVGGPQLVGNLLNYYYEYYYMVN
YLNPNVISISVTVPESFLAAYYPAMLDMIHNIMLQAAAQGISVLAASGDW
GYESDHPPPNFHIGTYNTIWYPESDPYVTSVGGIFLNASSNGSIVEISGW
DYSTGGNSVVYPAQIYEITSLIPFTPVIVRTYPDIAFVSAGGYNIPEFGF
GLPLVFQGQLFVWYGTSGAAPMTAAMVALAGTRLGALNFALYHISYQGII
ESPLGNFVGKVAWIPITSGNNPLPAHYGWNYVTGPGTYNAYAMVYDLLLY
SGLIES

An exemplary protease is Sso2037 comprising the amino acid sequence as follows:

(SEQ ID NO: 28)
MQFRKTFLFLNIHFPYVLRNTLLILLLLLPTPLLAISLPTGVVAYDGPIF
TNQVLGYVNITSLQAYNASGSKFGVPPYGASLQLNVMLQVNTSNEEYYFW
LQNVADFITNESKMFFSENIWNSTTPLAGINNVIGKGEIYSTSDLFSHSS
YYAYGTYYIKYDFPFSFYLIVNESHNNQGVYVSFGYVILQNGNITPPNPT
FYDTVFIPVNNLTSASIIIANQTTPNLNLGIITYLGSYLDAELVWGGFGN
GASTTFLNMSSYLALLYMKNGKWVPFSQVYNYGSDTAESTNNLRVTIAKN
GDAYVTIGKQNPGLLTTNFNPSIPGFLYLNISSKIPFLVNNIISRTFSGY
VSAPIKLGFFMNYSINSSSFAVLNGNYPSLIEPNVSWFKILNIIPNYTYY
YLVRVNSSIPVIGTINGKQITLNDTNWFAQGTQIKIVNYTYYNGSDERYV
ISSILPSLSFNISSPLNVTINTIKQYRVIINSDLPTYLNDKRVNGSIWIN
TGTIVKLSASIPFYEVGRFIGTYNLTLGGTIVVNKPIVEKLQLSINNLLL
EITAIIIVIVIIMLILRKRR

An exemplary protease is Sso1886 comprising the amino acid sequence as follows:

(SEQ ID NO: 29)
MLKHIVLVLLLLLLTPLVAISFPTGVVAYNGPICTNEVLGYANISSLLAY
NTSASQLGVPPYGASLQLNVMLEVNTSGGEYYFWLQNVADFITNESKVFF
GDNIWNSTTPFAGINNIVGKGEIYSTSDFFSHSSYYAYGTYYIKYNFPFS
FYLIINESYDTQGVYVSFGYVILQNGNISPPNPIFYDTVFIPIQNLSFAS
IIIANQTTPSANFGIVTYLGNYLDAELVWGGFGNGESTTFLNMSSYLALL
YMKSGEWVPFSQVYNYGSDTAESTNNLQVLIGKNGDAYVTIGRQNPGLLT
TKFNPSYPSFLYLNISSKIPFLLNKSLSHAFSGYVTTQIKLGFFKNYSIN
SSSFAVLNGNYPSLIEPNVSWFKVLNIIPNYTYYYLVKVNSQIPVIANVN
GKQITLNSTDWFAQGTQISILNYTYYNGSNERYIISSILPSSSFNVSLPL
NITLSTIKQYRVLVDSNLPVYLNGERVNGSVWINAGSSIQLSANVPFYEK
GIFTGTYNVTPGSIITVNGPIVETLILSINTELMGIVAVIVIAVVAIAIL
VLRRRR

An exemplary protease is Sso2194 comprising the amino acid sequence as follows:

(SEQ ID NO: 30)

MMYKVLLIIILLLPLSMPLSIPTTSQPSALAFPSGVTSYPLNTIIYTDFV
MGRINISYLNIGSSYLPGGEYFTTGNASLQLNAMVLGEYWAQNVILFHQI
SNNTFYATLIVNLWNLSGPFSNTTSNSLVYQGLGVICYQGPTFKVTLPLS
ISLFMEIVNSTLNFGYNINGQKGIYFRYPIIGLFQLGGLSLLGLPNDLEL
VWGGPGGGSVVFMNVSSIANLYYFNGNTLTIVPNAYSIGFDTAESAYGVK
VYSTFPSVFSPIVIETSGVNVPSVLWPIPPHVLVNQTSNKITVKLSISNK
SLSGQAVYLETGFPPSVISSAVTNSSGIAVFPNNNYSFYVVYFPGNFTLS
STYYFSSPILNSLSSKFRSYYQDLLNFLNSAQNSFKKGIKSVLSKQETSI
TTTTLTSTTSSSSQFGVNLYIVLYILAFVIGMVISAILIRFKL

An exemplary protease is Sso2181 comprising the amino acid sequence as follows:

(SEQ ID NO: 31)

MTWSIFLLILALSDIVLPLTITNINNQSITTLSPNYYLTVAIVFPPSNLT
LLQQYVQEHVILNQTQVEKLFIPTEEISKTLSQLRQSNISATSYMNVILA
SGTVSQLEKALNGKFYVYELNGKRFFEFFGSPVIPNAIVIGTNITSLILN
KPTTLYNVTQAVAYNALKPSQLLYAYNISWLHAHNITGKGTAIGILDFYG
NPYIQQQLQEFDKQYNIPNPPFFKIVPIGAYNPNNGISTGWAMEISLDVE
YAHVIAPDAGIVLYVANPNIPLPAIIAYIVQQDEVNVVSQSFGIPELYVD
LGLIPLSYVNSLMYEYWLGEVEGISFAAASGDAGGNGYNYFLAPQGSVIF
PASIPYVLAVGGSSVYIGGNKTMETAWSGESVLGASTGGYSTLFPAPWYQ
DSNGFRVVPDVVADANPYTGAFILYYYNQTYLVGGTSLATPIVSGIIDLM
TQSYGKLGFVNPFLYELRNTSALSPIGFGYNTPYYVNSSELNPVTGLGSI
NAGYLYQLLPKVIHSSSISVGVNNITYLDGQVVKVVANITGIRPSSVIGI
VYNGSSVVQQFSLSFNGTYWVGEFVAEGSGIEEVIVKAGNLEGSTYVTIG
YQAQFIFPPIALFPEPEPVPIVVQLIYPNGSLVRNPSNLTALIYKYDQMN
NKMSIISSVQLQRTSLINLSILGIQIESSYLTGVYQLPSNIISGVYFIKI
PNVFGFDEFVSGIYILDAVYPPVFTNPVVLSPGQNVTILAEALAIGSPNV
TVTFYNISGNKVYSIPVNAITYQNTLLYITQITLPKLKPGYYYVVTKAIY
NASNFTAEGVGLTQIYVSPYSLNVKVRIIPNNSIVYQNQQIYVIANITYP
NGTEVKYGSFSAIIVPSYLSSQFDNLQLQYSVPLTYINGSWIGQLEIPSG
SSTNSLGYSTYGISGYWDVYVEGISADGIPTNFPATLDVNTLSINPISPS
SQFVVLPYVYVSVFNGTIAFNEFIDKAIVVGHNATFINSIIRNLIVENGT
VTLINSKVQNVSLVNSEIIKINSTVGNNVNYITTIGNNHAKSSYPSLDSG
SILTIGIVLDIITIIALILIKRRKKFI

An exemplary protease is Sso0916 comprising the amino acid sequence as follows:

(SEQ ID NO: 32)

MKMKKSDIIIILFIALIYILMFSNIVQSASVEGVSMYPIFQNGALTFYVK
PISINEGNVIIYKSPYFNNYVIHRVIATDNGYYITQGVDKITNPIPDNRI
GLEPASGIPKNLVVGKIVEFGNFTFSIPYLGYISILFSSII

An exemplary protease is Sso1141 comprising the amino acid sequence as follows:

(SEQ ID NO: 33)

MYRYIFLMSMLLISIIPLVFASNPNMYQNPITLKEFREIGTLNANEEVIV
TIFVPLKNLDLLYYYASGASNPASPLYHKFLSPHEVQQLFLPTEEYNQIL
NYVKSSGFQVIFTASNSVIVIKGTVGQVEKYLGTKYAVYSNGSVTYYTNY
GYPKINAYVYSSNISAIFFAHPSTLITESTIKSFQQEINQTFPLEGYWPT
VLQKVYNVTTEGENTTIGILDFYGDPYIVQQLAYFDKITGLPNPPNFSVV
PIGPYNPNLGIVTGWAGEISLDVEVAHAIAPKANITLYIANPNIPLPAII
AYITSQNKVDTLSQSFSIPESLFSSLFNGPLFYSCIILSDEYYALGSAEG
ITFLASSGDAGGSGYSNGPIGTVGYPSTSPFVTSVGGTTVYVQFPNGSYY
QTAWSNYGFVPNNVNYGGSTGGVSIIEPKPWYQWGLPTPSTYPNGKLIPE
ISANANVYPGIYIVLPSNTTGITGGTSEASPLTAGVLATIESYTHHRIGL
LNPILTYMAENYYGKVIEPITFGYNIPWVATYGYNLVTGYGTINAGYFEK
ILPTLNLSKELNVIVSVYNTSIPTVSPQQFYPGQRILVTANITYPNGSPV
QTGEFKALIENYLGNLTTFNLTYNSLTKLWTGSGVLSNKASGILFVYVYG
SSDGLRGIGYYETFSGYYITFNYTTTFTPVYVELGNAELGITLSNSYFQA
PIGVMNITLNIYSYNITTNAYTFVTTLSVPIKNGVGVIDLPPDLSIGDLL
IIAEGNAYGFDAFTNGVYMQTLFILPQVVVEPGSVSPGQHITIEGSIIPP
VNLPSTTFQDALQGTNITAKLVSSNGVVINEANIPLSPNGIYFGYLYIPK
NTPSGLYNVLLFATYYSYTLNTTIRGFYYGQIYVSNQATISVKSVNYAFE
GQTVFIYANITNGTNEIKFGMFSATVYPSSLSFNYTTISSIIEIPLWYNP
KIGEWEGNFTLPSAISAGNLTYLAGQGYFGVPFKVLITGISALGNPTTTN
SGNAYTINVLPYTLFTNQTLDKTLPSYASLVNVKILNVSGNLLNDFLTNV
IIVNSNVKILNGNISNIVIRNSTVLIMQSNANNITLYNSTLYAIGGSING
LNVVNSKVVPINIHIQGLYPELPSISINLPSKNVTGTVNVTVNVIGEDVS
RINVYLNGNLINSFTTNGTHIVTINTQNYPDGGYNLTVTAIQSDGLSSSN
SSYLYFENGLTNLNTKVNVISNQLTNVSNSLSSSISSLRTASLEYQSISL
AIGIIAIVLAILALVRRRR

An exemplary protease is Sso1175 comprising the amino acid sequence as follows:

(SEQ ID NO: 34)

MYMKAKHLISLIVILTPLVTLLTSAVYTSGGITFYSPAYNGESYYTGQSI
TIDALLPQQFATDAATINFFFPNSSLAVTIPVQINGSGGIYVPNAYAFPN
VPGTWQITIEVAGGVAVGTINVNVIQRTPLVTVHLGYGVVGQALPQTPTI
TLTFPNGTTITVPLQGTVNVPSGTSYQVEQAITENNIRWATNYTSGTITP
ATTSITPTYYQQYLVTFNYTVQGGTGYSPPTVYYRSLGMNETAKAPASVW
VDANSAYIYSPELQSNVQGERWIAVNFTGIIKAPGEINEYYINQYLVTVQ
SQIPVYAIVNGANETLNSTNWFTQGTTIKLENITKYVSSVERYVIANFSP

-continued

SEVITVNQPTTIKVNTVTQYFINVNSPVQLKALINGANESLTAGWYNQGT

SIKIENLTYYVGNGERLILGKVLPSLEIIVNGSYTISTTTITQYFVNVSS

PIPVQVLINGSKTILNSSWINAGTSILVLNYTYNISPQERVIIVGISPSQ

SFTVNSPETLKLLTVTQYLVTINGVSKFYNSGSKIVLNASVPFYETATFK

GTYNVSPGATITVNQPITETLVESPNYLILGAIAAVIIIVVAVVVIILLR

R

An exemplary protease is Saci_1714 (Lin et al., *J Biol Chem.* 1990 Jan. 25; 265(3):1490-5) comprising the amino acid sequence as follows:

(SEQ ID NO: 35)

MNFKSICLIILLSALIIPYIPQNIYFFPHRNTTGATISSGLYVNPYLYYT

SPPAPAGIASFGLYNYSGNVTPYVITTNEMLGYVNITSLLAYNREALRYG

VDPYSATLQFNIVLSVNTSNGVYAYWLQDVGQFQTNKNSLTFIDNVWNLT

GSLSTLSSSAITGNGQVASAGGGQTFYYDVGPSYTYSFPLSYIYIINMSY

TSNAVYVWIGYEIIQIGQTEYGTVNYYDKITIYQPNIISASLMINGNNYT

PNGLYYDAELVWGGGGNGAPTSFNSLNCTLGLYYISNGSITPVPSLYTFG

ADTAEAAYNVYTTMNNGVPIAYNGIENLTILTNNFSVILI

In some embodiments, the method comprises: (a) culturing the host cell in a suitable medium comprising a hemicellulose, or component thereof, as essentially the sole carbon source, and the peptide or protein of interest encoded in the nucleic acid is an enzyme described in one of the references cited earlier, such that the enzyme is expressed. In some embodiments, the nucleic acid encodes two, three, or more than three such enzymes and these enzymes are expressed.

In some embodiments, the culturing step comprises culturing the host cell in a medium having a temperature of equal to or more than about 70° C., 75° C., 80° C., 85° C., or 90° C. In some embodiments, the culturing step comprises culturing the host cell in a medium having a pH of equal to or less than about 4.0, 3.5, 3.0, 2.5, or 2.0. In some embodiments, the culturing step comprises culturing the host cell in a medium having a temperature of equal to or more than about 70° C., and a pH of equal to or less than about 4.0. In some embodiments, the culturing step comprises culturing the host cell in a medium comprising lignocellulosic or cellulosic biomass, such as switchgrass, bagasse, corn-stover, or forestry waste material. In some embodiments, the culturing step comprises culturing the host cell in a medium comprising lignocellulosic or cellulosic biomass, such as switchgrass, bagasse, corn-stover, or forestry waste material, at a temperature of equal to or more than about 70° C., and a pH of equal to or less than about 4.0. In some embodiments, the lignocellulosic or cellulosic biomass is essentially the sole carbon source in the medium.

In some embodiments, the novel vector is constructed using a Gateway® (Invitrogen) destination cassette inserted into the cloning vector for *Sulfolobus solfataricus*. Our cloning strategies employ PCR targeting and amplification of genes of interest using primers containing small inducible promoters to rapidly and efficiently clone and express recombinant genes. Recombinant proteins show native localization and modification and can be genetically targeted for secretion, membrane association or integration, and extracellular accumulation. These tools can be applied to generate cellulase enzymes that are active on cellulosic plant material in dilute sulfuric acid at elevated temperatures and acidic pH. The vectors of the present invention are useful in exploring extremophilic genomes and exploiting their useful gene products and their acid, heat, and detergent stability characteristics for industrial and energy applications.

Sulfolobus is used as a model system for genetics and microbiology of archaeal hyperthermophiles and acidophiles. Currently the economical degradation of cellulosic materials to liberate sugars for fermentation into ethanol is a major barrier to producing practical biofuels. Proteins from archaea and extremophilic bacteria have many practical applications as their enzymes are hyper-stable and can tolerate extreme conditions like those used in industrial processes. The present invention enables practical and efficient molecular genetics for this organism to generate acid and/or heat and detergent stable enzymes from archaea and bacteria.

Lignocellulosic Pretreatment Conditions Compatible with *Sulfolobus* Growth

Currently, one of the most efficient means to degrade cellulose into component sugars is the use of sulfuric acid and high (about 250° C.) temperatures, using chemical hydrolysis to liberate fermentable sugars. Alternatively, enzymatic hydrolysis produces fewer detrimental side-products but requires a feedstock pretreatment. Pretreatment typically involve exposure to dilute sulfuric acid at elevated temperatures (about 120° C.). *Sulfolobus* thrives in dilute sulfuric acid at relatively high temperatures (80° C.). *Sulfolobus* Growth media is a media sufficient for lignocellulosic feedstock pre-treatment to facilitate enzymatic saccharification (see FIGS. **6-9** and Tables 1 and 2). The present invention enables an integrated pretreatment/enzyme production/saccharification process, where lignocellulosic pretreatment, enzyme production, and enzymatic degradation under hot acidic conditions occur concurrently.

TABLE 1

List of recombinant heat and acid stable cellulase enzymes produced in *Sulfolobus* and their activities on relevant cellulosic substrates.

	Cellulolytic Activity			Hemicellulolytic Activity							
Protein	Azo-CMC	PNP-B-D-Cellobloside	PNP-B-D-Glucopy-ranoside	RBB-Xylan	PNP-B-D-Xylopyranoside	PNP-B-D-Glucuronide	PNP-A-L-Arabi-nofuranoside	Optima			*E. coli*
Gene #	Endo-	Biosidase	Biosidase	Endo-	Biosidase	Biosidase	Biosidase	pH	T	½ Life	Expres-sion
Sso1353	–	+	++	–	++	+	++	6.0	90° C.	2.2 h	Active
Sso1354	+++	–	–	+++	–	–	–	3.6	90° C.	5.5 h	NOT active
Sso3007	–	–	++	–	–	–	+	6.5	80° C.	2.5 h	NOT active

TABLE 1-continued

List of recombinant heat and acid stable cellulase enzymes produced in *Sulfolobus* and their activities on relevant cellulosic substrates.

	Cellulolytic Activity			Hemicellulolytic Activity							
Protein	Azo-CMC	PNP-B-D-Cellobloside	PNP-B-D-Glucopy-ranoside	RBB-Xylan	PNP-B-D-Xylopyranoside	PNP-B-D-Glucuronide	PNP-A-L-Arabi-nofuranoside	Optima			*E. coli* Expres-
Gene #	Endo-	Biosidase	Biosidase	Endo-	Biosidase	Biosidase	Biosidase	pH	T	½ Life	sion
Sso3019	–	+	+++	–	+	+	–	6.8	80° C.	0.85 h	ND
Sso3032	–	–	++	–	+++	–	++++	6.8	70° C.	10.5 h	Active
Sso3036	–	–	–	–	–	++++	–	6.8	90° C.	7 h	ND

Notably two of these six enzymes are inactive when produced in eubacterial strains.

Sulfolobus Growth media and lignocellulosic pretreatment solution comprise the following ingredients listed in Table 3.

TABLE 2

Ingredients of Sulfolobus Growth media and lignocellulosic pretreatment solution.

Ingredient	Final concentration
Ammonium sulfate	0.30%
Glycine	0.07%
Potassium hydrogen phosphate	0.05%
Potassium chloride	0.01%
Sodium borate	0.000002440%
Manganese chloride	0.000000900%
Zinc sulfate	0.000000110%
Cupric sulfate	0.000000025%
Sodium molybdate	0.000000015%
Vandyl sulfate	0.000000015%
Cobalt chloride	0.000000005%
Nickel sulfate	0.000000005%
Magnesium chloride	1 mM
Calcium nitrate	0.3 mM

The nucleic acid can further comprise a ribosomal binding site. The inclusion of a ribosomal binding site between multiple independently transcribed genes has been used to cause high-level expression of two genes simultaneously. Two or more genes assembled into an artificial polycistronic message can be expressed as proteins by inclusion of a ribosomal binding site between the two genes. The sequence of such a ribosomal binding site is: gaggtgagtcgga (SEQ ID NO:24).

Particular embodiments of the invention include, but are not limited to, the following:

A recombinant or isolated nucleic acid comprising: (a) a nucleotide sequence that is capable of stably integrating into the chromosome of an Archea or acidophilic hyperthermophilic eubacteria, and (b) a nucleotide sequence of interest. In some embodiments, the nucleic acids described above wherein the nucleotide sequence of interest comprises a single or multiple cloning site or a sequence to direct targeted integration via enzymatic processes. In some embodiments, the nucleic acids described above wherein the Archaea or eubacteria is hyperthermophilic. In some embodiments, the nucleic acids described above wherein the Archaea or eubacteria is capable of growth or is viable at a temperature equal to or more than about 70° C., 75° C., 80° C., 85° C., or 90° C. In some embodiments, the nucleic acids described above wherein the Archaea is capable of growth or is viable at a temperature equal to 80° C. In some embodiments, the nucleic acids described above wherein the Archaea or eubacteria is an acidophilic Archaea. In some embodiments, the nucleic acids described above wherein the Archaea or eubacteria is capable of growth or is viable at a pH equal to or less than about 4.0, 3.5, 3.0, 2.5, or 2.0. In some embodiments, the nucleic acids described above wherein the Archaea is capable of growth or is viable at a pH within the range of from about 2.0 to about 3.0. In some embodiments, the nucleic acids described above wherein the Archaea is of the kingdom Crenarchaeota. In some embodiments, the nucleic acids described above wherein the Archaea of the phylum Crenarchaeota. In some embodiments, the nucleic acids described above wherein the Archaea is of the class Thermoprotei. In some embodiments, the nucleic acids described above wherein the Archaea is of the order Sulfolobales. In some embodiments, the nucleic acids described above wherein the Archaea is of the family Sulfolobaceae. In some embodiments, the nucleic acids described above wherein the Archaea is of the genus *Sulfolobus*. In some embodiments, the nucleic acids described above wherein the Archaea is *Sulfolobus solfataricus, Sulfolobus islandicus, Sulfolobus acidocaldarius, Sulfolobus tokodaii, Metallosphaera yellowstonensis, Metallosphaera sedula*, or *Acidianus brierleyi*. In some embodiments, the nucleic acids described above wherein the nucleotide sequence that is capable of stably integrating into a chromosome of a *Sulfolobus* species. In some embodiments, the nucleic acids described above wherein the nucleotide sequence that is capable of stably integrating into the chromosome is the integration sequence of a Fusellovirus capable of infecting a *Sulfolobus* species. In some embodiments, the nucleic acids described above wherein the Fusellovirus is a *Sulfolobus* spindle-shaped virus. In some embodiments, the nucleic acids described above wherein the *Sulfolobus* spindle-shaped virus is SSV1, SSV2, SSV3, SSVL1, SSVK1, or SSVRH. In some embodiments, the nucleic acids described above wherein the nucleotide sequence that is capable of stably integration into the chromosome comprises the nucleotide sequence of SEQ ID NO:1-9. In some embodiments, the nucleic acids described above wherein the nucleotide sequence of interest encodes a peptide, protein or RNA, or a DNA sequence that binds a protein. In some embodiments, the nucleic acids described above wherein the nucleic acid further comprising a promoter operably linked to the nucleotide sequence encoding the peptide, protein or RNA. In some embodiments, the nucleic acids described above wherein the peptide or peptide comprises an export peptide signal at the 5' end of the peptide or protein. In some embodiments, the nucleic acids described above wherein the export peptide signal comprises an amino acid sequence encoded by a XPO, SP, Seq1, Seq2, Seq3, Seq4, or Seq5 nucleotide sequence. In some embodiments, the nucleic acids described above wherein the protein

or peptide needs to be expressed, synthesized and/or folded at a temperature equal to or more than about 70° C., 75° C., 80° C., 85° C., or 90° C. in order to be correctly folded in order to be biological active. In some embodiments, the nucleic acids described above wherein the protein or peptide needs to be glycosylated or otherwise modified after translation by the host organism during or after expression, synthesis and/or folding in order to be biologically or biochemically active. In some embodiments, the nucleic acids described above wherein the resulting protein or peptide is stable in a detergent, or mixture thereof, such as Triton X-100, sodium dodecyl sulfate, or the like. In some embodiments, the nucleic acids described above wherein the protein or peptide is a cellulase or protease. In some embodiments, the nucleic acids described above wherein the nucleic acid further comprises one or more control sequences which permit stable maintenance of the nucleic acid as a vector in a non-*Sulfolobus* host cell. In some embodiments, the nucleic acids described above wherein the control sequence is a sequence comprising an origin of replication (ori) functional in *Escherichia coli* cells.

An Archaea host cell comprising the nucleic acid of the present invention stably integrated into the chromosome of the host cell. In some embodiments, the host cell described above wherein the nucleic acid of present invention as an extrachromosomal element in the host cell. In some embodiments, the host cell described above wherein the host cell is hyperthermophilic. In some embodiments, the host cell described above wherein the host cell is capable of growth or is viable at a temperature equal to or more than about 70° C., 75° C., 80° C., 85° C., or 90° C. In some embodiments, the host cell described above wherein the host cell is capable of growth or is viable at a temperature equal to 80° C. In some embodiments, the host cell described above wherein the host cell is acidophilic. In some embodiments, the host cell is capable of growth or is viable at a pH equal to or less than about 4.0, 3.5, 3.0, 2.5, or 2.0. In some embodiments, the host cell described above wherein the host cell is capable of growth or is viable at a pH within the range of from about 2.0 to about 6.0. In some embodiments, the host cell described above wherein the Archaea is of the kingdom Crenarchaeota. In some embodiments, the host cell described above wherein the Archaea is of the phylum Crenarchaeota. In some embodiments, the host cell described above wherein the Archaea is of the class Thermoprotei. In some embodiments, the host cell described above wherein the Archaea is of the order Sulfolobales. In some embodiments, the host cell described above wherein the Archaea is of the family Sulfolobaceae. In some embodiments, the host cell described above wherein the Archaea is of the genus *Sulfolobus*. In some embodiments, the host cell described above wherein the Archaea is *Sulfolobus solfataricus, Sulfolobus islandicus, Sulfolobus acidocaldarius, Sulfolobus tokodaii, Metallosphaera yellowstonensis, Metallosphaera sedula*, or *Acidianus brierleyi*. In some embodiments, the host cell described above wherein the nucleotide sequence of interest encodes a peptide, protein or RNA, and the peptide, protein or RNA is heterologous to the host cell.

A method of constructing the host cell of the present invention, comprising: (a) introducing a nucleic acid comprising: (i) a nucleotide sequence that is capable of stably integrating into the chromosome of a host cell that is an Archea or acidophilic hyperthermophilic eubacteria, and (ii) a nucleotide sequence of interest into an Archaea host cell, and (b) integrating the nucleic acid into a chromosome of the host cell or (c) maintaining the nucleic acid as an extrachromosomal element. In some embodiments, the method described above wherein the nucleic acid is a nucleic acid described above. In some embodiments, the method described above wherein the host cell is a host cell described above.

A method of expressing a peptide or protein or RNA of interest in an Archaea, comprising: (a) optionally constructing the nucleic acid of one of the present invention, (b) optionally introducing the nucleic acid into an Archaea host cell, (c) optionally integrating the nucleic acid into a chromosome of the host cell, (d) culturing the host cell in a suitable medium such that a peptide or protein or RNA of interest encoded in the nucleic acid is expressed, and (e) optionally isolating the peptide or protein or RNA from the host cell, (f) designing the nucleic acid such that a peptide or protein or RNA of interest encoded in the nucleic acid is targeted to the membrane, intrcellular or extracellular compartment and modified by glycosylation of other post-translational process as part of this cellular targeting. In some embodiments, the method described above wherein the peptide or protein of interest is a thermophilic enzyme, or enzymatically active fragment thereof, capable of catalyzing an enzymatic reaction. In some embodiments, the method described above wherein the peptide or protein of interest is a cellulase. In some embodiments, the method described above wherein the enzymatic reaction is an enzymatic degradation or catabolic reaction. In some embodiments, the method described above wherein the medium comprises a pretreated biomass. In some embodiments, the method described above wherein the nucleic acid is a nucleic acid described above. In some embodiments, the method described above wherein the host cell is a host cell described above.

REFERENCES CITED

1. Jenney F E, Jr., Adams M W. The impact of extremophiles on structural genomics (and vice versa). Extremophiles : life under extreme conditions. 2008;12(1):39-50.
2. Noll K M, Vargas M. Recent advances in genetic analyses of hyperthermophilic archaea and bacteria. Archives of microbiology. 1997;168(2):73-80.
3. Allers T, Mevarech M. Archaeal genetics—the third way. Nature reviews Genetics. 2005;6(1):58-73.
4. Lipscomb G L, Stirrett K, Schut G J, Yang F, Jenney F E, Jr., Scott R A, Adams M W, Westpheling J. Natural competence in the hyperthermophilic archaeon Pyrococcus furiosus facilitates genetic manipulation: construction of markerless deletions of genes encoding the two cytoplasmic hydrogenases. Applied and environmental microbiology. 2011;77(7):2232-8. PMCID: 3067412.
5. Hopkins R C, Sun J, Jenney F E, Jr., Chandrayan S K, McTernan P M, Adams M W. Homologous expression of a subcomplex of Pyrococcus furiosus hydrogenase that interacts with pyruvate ferredoxin oxidoreductase. PloS one. 2011;6(10):e26569. PMCID: 3200332.
6. Chandrayan S K, McTernan P M, Hopkins R C, Sun J, Jenney F E, Jr., Adams M W. Engineering Hyperthermophilic Archaeon Pyrococcus furiosus to Overproduce Its Cytoplasmic [NiFe]-Hydrogenase. The Journal of biological chemistry. 2012;287(5):3257-64. PMCID: 3270980.
7. Bridger S L, Clarkson S M, Stirrett K, DeBarry M B, Lipscomb G L, Schut G J, Westpheling J, Scott R A, Adams M W. Deletion strains reveal metabolic roles for key elemental sulfur-responsive proteins in Pyrococcus furiosus. Journal of bacteriology. 2011;193(23):6498-504. PMCID: 3232869.

8. Kurosawa N, Grogan D W. Homologous recombination of exogenous DNA with the *Sulfolobus* acidocaldarius genome: properties and uses. FEMS microbiology letters. 2005;253(1):141-9.
9. Albers S V, Driessen A J. Conditions for gene disruption by homologous recombination of exogenous DNA into the *Sulfolobus* solfataricus genome. Archaea. 2008;2(3): 145-9. PMCID: 2685593.
10. Berkner S, Lipps G. Genetic tools for *Sulfolobus* spp.: vectors and first applications. Archives of microbiology. 2008;190(3):217-30.
11. Albers S V, Jonuscheit M, Dinkelaker S, Urich T, Kletzin A, Tampe R, Driessen A J, Schleper C. Production of recombinant and tagged proteins in the hyperthermophilic archaeon *Sulfolobus* solfataricus. Applied and environmental microbiology. 2006;72(1):102-11. PMCID: 1352248.
12. Dworkin M, Falkow S. The prokaryotes : a handbook on the biology of bacteria. 3rd ed. New York ; London: Springer; 2006.
13. Jonuscheit M, Martusewitsch E, Stedman K M, Schleper C. A reporter gene system for the hyperthermophilic archaeon *Sulfolobus* solfataricus based on a selectable and integrative shuttle vector. Molecular microbiology. 2003; 48(5):1241-52.
14. Elferink M G, Schleper C, Zillig W. Transformation of the extremely thermoacidophilic archaeon *Sulfolobus* solfataricus via a self-spreading vector. FEMS microbiology letters. 1996;137(1):31-5.
15. Cannio R, Contursi P, Rossi M, Bartolucci S. An autonomously replicating transforming vector for *Sulfolobus* solfataricus. Journal of bacteriology. 1998;180(12): 3237-40. PMCID: 107829.
16. Aucelli T, Contursi P, Girfoglio M, Rossi M, Cannio R. A spreadable, non-integrative and high copy number shuttle vector for *Sulfolobus* solfataricus based on the genetic element pSSVx from *Sulfolobus* islandicus. Nucleic acids research. 2006;34(17):e114. PMCID: 1635272.
17. Leigh J A, Albers S V, Atomi H, Allers T. Model organisms for genetics in the domain Archaea: methanogens, halophiles, Thermococcales and Sulfolobales. FEMS microbiology reviews. 2011;35(4):577-608.
18. Martin A, Yeats S, Janekovic D, Reiter W D, Aicher W, Zillig W. SAV 1, a temperate u.v.-inducible DNA virus-like particle from the archaebacterium *Sulfolobus* acidocaldarius isolate B12. The EMBO journal. 1984;3(9): 2165-8. PMCID: 557659.
19. Schleper C, Kubo K, Zillig W. The particle SSV1 from the extremely thermophilic archaeon *Sulfolobus* is a virus: demonstration of infectivity and of transfection with viral DNA. Proceedings of the National Academy of Sciences of the United States of America. 1992;89(16):7645-9. PMCID: 49767.
20. Martusewitsch E, Sensen C W, Schleper C. High spontaneous mutation rate in the hyperthermophilic archaeon *Sulfolobus* solfataricus is mediated by transposable elements. Journal of bacteriology. 2000;182(9):2574-81. PMCID: 111323.
21. Lubelska J M, Jonuscheit M, Schleper C, Albers S V, Driessen A J. Regulation of expression of the arabinose and glucose transporter genes in the thermophilic archaeon *Sulfolobus* solfataricus. Extremophiles : life under extreme conditions. 2006;10(5):383-91.
22. Hopp T P, Prickett K S, Price V L, Libby R T, March C J, Cerretti D P, Urdal D L, Conlon P J. A Short Polypeptide Marker Sequence Useful for Recombinant Protein Identification and Purification. Bio-Technol. 1988;6(10): 1204-10.
23. Bradford M M. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Analytical biochemistry. 1976;72:248-54.
24. Brizzard B. Epitope tagging. BioTechniques. 2008;44 (5):693-5.
25. Yoon S H, Reiss D J, Bare J C, Tenenbaum D, Pan M, Slagel J, Moritz R L, Lim S, Hackett M, Menon A L, Adams M W, Barnebey A, Yannone S M, Leigh J A, Baliga N S. Parallel evolution of transcriptome architecture during genome reorganization. Genome research. 2011;21(11):1892-904. PMCID: 3205574.
26. Lund P. Insights into chaperonin function from studies on archaeal thermosomes. Biochemical Society transactions. 2011;39(1):94-8.
27. Zhang Y, Buchholz F, Muyrers J P, Stewart A F. A new logic for DNA engineering using recombination in *Escherichia coli*. Nature genetics. 1998;20(2):123-8.
28. Degryse E. Evaluation of *Escherichia coli* recBC sbcBC mutants for cloning by recombination in vivo. Journal of biotechnology. 1995;39(2):181-7.
29. Trent J D, Kagawa H K, Yaoi T, Olle E, Zaluzec N J. Chaperonin filaments: the archaeal cytoskeleton? Proceedings of the National Academy of Sciences of the United States of America. 1997;94(10):5383-8. PMCID: 24687.
30. Cannio R, D'Angelo A, Rossi M, Bartolucci S. A superoxide dismutase from the archaeon *Sulfolobus* solfataricus is an extracellular enzyme and prevents the deactivation by superoxide of cell-bound proteins. European journal of biochemistry/FEBS. 2000;267(1):235-43.
31. Ursby T, Adinolfi B S, Al-Karadaghi S, De Vendittis E, Bocchini V. Iron superoxide dismutase from the archaeon *Sulfolobus* solfataricus: analysis of structure and thermostability. Journal of molecular biology. 1999;286(1):189-205.
32. Szabo Z, Sani M, Groeneveld M, Zolghadr B, Schelert J, Albers S V, Blum P, Boekema E J, Driessen A J. Flagellar motility and structure in the hyperthermoacidophilic archaeon *Sulfolobus* solfataricus. Journal of bacteriology. 2007;189(11):4305-9.

The above references are hereby incorporated by reference.

It is to be understood that, while the invention has been described in conjunction with the preferred specific embodiments thereof, the foregoing description is intended to illustrate and not limit the scope of the invention. Other aspects, advantages, and modifications within the scope of the invention will be apparent to those skilled in the art to which the invention pertains.

All patents, patent applications, and publications mentioned herein are hereby incorporated by reference in their entireties.

The invention having been described, the following examples are offered to illustrate the subject invention by way of illustration, not by way of limitation.

EXAMPLE 1

Recombinant Acid/Heat Stable Cellulases in *Sulfolobus solfataricus*

Potential applications for acid/thermal-stable enzymes in industrial processes have long been recognized and initiated

much interest in acidophilic and hyperthermophilic microbes such as the archaeal *Sulfolobales*. Here we report the development of an efficient and rapid means to produce recombinant acid/thermal-stable proteins that are highly resistant to detergent denaturation at high levels with *Sulfolobus solfataricus*. Building on previous works with *Sulfolobus* vectors, we have developed a PCR-based cloning approach to modify, express, target localization, and purify recombinant proteins from *Sulfolobus solfataricus*. Novel vectors are used here to generate over 80 *Sulfolobus* expression constructs with various affinity tags for detection, quantification, and purification. We define minimal promoters that can be incorporated into PCR primers to facilitate inducible protein expression over a >1500 fold range and yielding over 2.5 mg per liter of cell culture. Polycistronic co-expression of the alpha and gamma subunits of the thermosome yields protein levels approaching 5% of the total cell protein. We show recombinant protein localization to the intracellular, membrane, or extracellular compartments. An intracellular ATPase is efficiently targeted for secretion by inclusion of a small leader peptide. Finally, we use our vectors to generate active acid/heat stable cellulases that are highly glycosylated and secreted from *Sulfolobus* cells. We show the production of cellulolytic enzymes in *Sulfolobus* and degradation of lignocellulosic feedstocks with these enzymes. We also show production of xylose from plant xylan and glucose and xylan from raw switchgrass biomass in a single-step pretreatment-saccharification process. In addition we show the ability to mix multiple enzymes to alter the sugar products form plant lignocellulose in dilute sulfuric acid at high temperatures in these single-step pretreatment-saccharification reactions. These compsitions and methods have uses in industrial and bioenergy applications.

Construction of high-throughput expression vectors for *Sulfolobus solfataricus*. Vectors were built from established shuttle vectors and based on the *Sulfolobus* viral pathogen SSV1 (Martin, A., et al. SAV 1, a temperate u.v.-inducible DNA virus-like particle from the archaebacterium *Sulfolobus* acidocaldarius isolate B12. The *EMBO journal* 3, 2165-2168 (1984); Schleper, C., Kubo, K. & Zillig, W. The particle SSV1 from the extremely thermophilic archaeon *Sulfolobus* is a virus: demonstration of infectivity and of transfection with viral DNA. *Proceedings of the National Academy of Sciences of the United States of America* 89, 7645-7649 (1992)). The starting plasmid for this work was plasmid PMJ05, a derivative of the PMJ03 shuttle vector, which is effectively a pUC18 *E. coli* vector integrated into a SSV1 viral genome (Jonuscheit, M., Martusewitsch, E., Stedman, K. M. & Schleper, C. A reporter gene system for the hyperthermophilic archaeon *Sulfolobus* solfataricus based on a selectable and integrative shuttle vector. *Molecular microbiology* 48, 1241-1252 (2003); Martusewitsch, E., Sensen, C. W. & Schleper, C. High spontaneous mutation rate in the hyperthermophilic archaeon *Sulfolobus solfataricus* is mediated by transposable elements. *Journal of bacteriology* 182, 2574-2581 (2000)). The PMJ-vectors were designed with the PyrEF genes as selectable markers that complement uracil auxotrophy in the *Sulfolobus* PH1-16 strain (Albers, S. V., et al. Production of recombinant and tagged proteins in the hyperthermophilic archaeon *Sulfolobus solfataricus*. *Applied and environmental microbiology* 72, 102-111 (2006)). Limited use of the PMJ05 and related plasmids for recombinant protein expression and tagging of proteins in *Sulfolobus* has been demonstrated (Albers, S. V., et al. (2006)). To expand recombinant capabilities in *Sulfolobus*, we first replaced the tf55 promoter and LacS genes with either the AraS or tf55 promoter from *Sulfolobus* and the Gateway® destination-cassette (Invitrogen) to generate the pSMY-A and pSMY-T vectors respectively (FIG. **1** Panel a). An additional vector was constructed by cloning the destination cassette into the same sites producing the promoter-less pSMY1 vector. All three vectors were propagated in *E. coli*, purified, and sequenced prior to further experimentation in *Sulfolobus*. For all experiments the pSMY vectors were electroporated into the PH1-16 strain of *Sulfolobus* and selected in liquid and on plates to validate vector stability and selectable marker function in *Sulfolobus* as previously described (Schleper, C., et al. (1992); Albers, S. V., et al. (2006)).

The strategy for cloning and tagging genes of interest into the pSMY *Sulfolobus* expression vectors involves; 1) PCR amplification and modification of target genes using primers encoding promoters and/or epitope fusion tags, 2) direct cloning of the PCR products using TOPO° vectors (Invitrogen), and 3) in vitro recombination of the genes of interest into the *Sulfolobus* expression vectors (FIG. **1** Panel b). Validated reaction products are then transferred into the uracil auxotrophic strain of *Sulfolobus* (PH1-16) by electroporation and selected in media lacking uracil. The entire cloning process nominally requires ten days from PCR reactions to detectable protein expression in *Sulfolobus*.

Construction of high-throughput expression vectors for *Sulfolobus solfataricus*. Vectors were built from established shuttle vectors and based on the *Sulfolobus* viral pathogen SSV1 (18, 19). The starting plasmid for this work was plasmid PMJ05, a derivative of the PMJ03 shuttle vector, which is effectively a pUC18 *E. coli* vector integrated into a SSV1 viral genome (13, 20). The PMJ-vectors were designed with the PyrEF genes as selectable markers that complement uracil auxotrophy in the *Sulfolobus* PH1-16 strain (11). Limited use of the PMJ05 and related plasmids for recombinant protein expression and tagging of proteins in *Sulfolobus* has been demonstrated (11). To expand recombinant capabilities in *Sulfolobus*, we first replaced the tf55 promoter and LacS genes with either the AraS or tf55 promoter from *Sulfolobus* and the Gateway® destination-cassette (Invitrogen) to generate the pSMY-A and pSMY-T vectors respectively (FIG. **1** Panel a). An additional vector was constructed by cloning the destination cassette into the same sites producing the promoter-less pSMY1 vector. All three vectors were propagated in *E. coli*, purified, and sequenced prior to further experimentation in *Sulfolobus*. For all experiments the pSMY vectors were electroporated into the PH1-16 strain of *Sulfolobus* and selected in liquid and on plates to validate vector stability and selectable marker function in *Sulfolobus* as previously described (11, 19).

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Quantitative analysis of expression from inducible *Sulfolobus* promoters. Four different *Sulfolobus* promoter sequences were designed and evaluated to establish optimal promoters to regulate protein expression levels. The ther-

mosome α subunit promoter (tf55) and the arabinose sugar transporter operon promoters (AraS) have been used previously for recombinant protein expression in *Sulfolobus* (11, 21). To simplify the addition of inducible promoters to genes of interest using PCR, we designed 'minimal' 61 nucleotide versions of the tf55 and AraS promoters (FIG. **2** Panel A). Expression vectors driven by the four varied promoters were constructed with identical FLAG-Sso0287 coding sequences to test promoter functions in *Sulfolobus*. The Sso0287 gene encodes a 68 kDa cytoplasmic protein with unknown cellular functions and has previously been expressed in *Sulfolobus* using a related viral vector (11). Immunoblotting was used to evaluate the relative expression and induction levels among these four constructs (Fig.2 Panel B). The basal expression and inducibility of the various promoters was evaluated after 72 hours of growth under standard and inducing conditions (80 or 85° C. for tf55 constructs and +/−10 uM D-arabinose for AraS constructs). Both the full length and the 'minimal' AraS promoters were tightly controlled by D-arabinose under our experimental conditions (FIG. **2** Panel B). Notably, the minimal AraS promoter (61 base) appeared to have lower levels of baseline expression and higher expression after induction relative to the longer (303 base) AraS promoter. Likewise, the minimal tf55 promoter constructs appeared to have markedly higher expression levels than the larger promoter. In contrast to the AraS promoters, neither tf55 promoter showed inducible expression under our experimental conditions (FIG. **2** Panel B).

To further validate these results and establish whether promoters were the primary factor determining recombinant protein levels, we generated twelve additional expression constructs with four promoters driving three different genes. Constructs were generated for each of the four promoters described above, driving expression of; 1) RNA helicase (Sso1440), 2) cell division control protein 6 (cdc6) (Sso 0771), and 3) DNA polymerase subunit D (Sso0071). Sequence-validated constructs were electroporated into the *Sulfolobus* PH1-16 strain and protein levels evaluated by FLAG-immunoblots under inducing conditions (FIG. **2** Panel C). Protein levels for these 12 constructs were largely in concurrence with the FLAG-Sso0287 expression levels with the four promoters (FIG. **2** Panel B). More specifically, the relative expression levels under inducing conditions was; a>t>T≈A with relatively small variations between proteins (FIG. **2** Panel C). In nearly all cases Sso0771 protein had accumulated to greater levels than the other proteins, but the promoter appeared to be the principal determinant for protein levels in *Sulfolobus*. Notably, the 61-nucleotide AraS promoter retains inducibility and the smaller versions of both promoters show significantly higher expression than their larger counterparts. Such minimal promoters can likewise be derived from other genes and species for application to the production of hyper-stable proteins, RNAs and enzymes.

Recombinant protein yields greater than one milligram per liter in *Sulfolobus*. To quantify recombinant protein expression levels in *Sulfolobus*, three recombinant proteins (Sso0316, Sso0071, and Sso07710) were purified to near homogeneity using immunoaffinity chromatography and protein concentrations determined by Bradford assays (22, 23). Serial dilutions of pure proteins were used to establish the linear range of FLAG-immunoblot luminosity and molar protein amounts (FIG. **2** Panel D). Notably, all three FLAG-fusion proteins showed a consistent relationship between luminosity and molar protein amounts. Aliquots of purified FLAG-fusion protein standards were included on all subsequent immunoblots to calibrate luminosity to molar protein amounts. This approach was used to quantify protein expression levels of the Sso0287 protein driven by the promoters shown in FIG. **2** Panel B. The induction of Sso0287 protein was maximal under the control of the 61-nucleotide AraS promoter and was over 1500-fold relative to the control. Protein yields over 1.5 milligrams of protein per liter of *Sulfolobus* culture were observed (Table 3). Surprisingly, the control of protein expression was markedly greater for the minimal AraS promoter than the longer DNA sequences used previously (11).

TABLE 3

Promoter	Induction	Expression (ug/L)	Fold Induction
A	−	4.2	297.4
	+	1243.9	
a	−	1.0	1535.9
	+	1576.5	
T	−	33.6	1.7
	+	57.6	
t	−	635.1	1.0
	+	632.8	

Co-expression of multiple genes from polycistronic constructs. Many proteins function as members of assemblies and are transcribed and translated from single polycistronic mRNAs. Such proteins often show reduced stability and function when overexpressed as individual polypeptides and can be particularly difficult to produce in heterologous hosts such as *E. coli*. We therefore generated a polycistronic expression construct to evaluate protein co-expression with our vectors. The polycistronic Sso0888-0889 genes encode tryptophan synthase subunits beta and alpha respectively and were amplified from genomic DNA using PCR designed to add an inducible promoter and a Myc or FLAG epitope tag (24) to Sso0888 and Sso0889 respectively (FIG. **3** Panel A). The cloning and tagging strategy was identical that described above but in this case PCR primers encoded amino-terminal fused Myc tag on the first gene (Sso0888) and a carboxyl-terminal fused FLAG epitope on the downstream gene (Sso0889). This strategy permits simultaneous and exclusive detection of each gene product by immunoblotting. Like the individually expressed genes, the polycistronic genes 0888-0889 showed tightly controlled and inducible expression behind the minimal AraS minimal promoter with no evidence of *Sulfolobus* proteins being reactive with these antibodies (FIG. **3** Panel B).

To establish the general utility of this approach, three additional polycistronic operons were constructed; 1) the operon encoding the hypothetical proteins Sso0197 which has conserved kinase domains and Sso0198, 2) the operon encoding the DNA repair protein Sso2250 and the co-transcribed hypothetical gene Sso2251, and 3) the ferredoxin oxidoreductase subunits alpha and beta encoded by Sso2815 and Sso2816 respectively. These constructs all expressed recombinant tagged proteins from both members of the polycistronic messages at approximately equal levels (FIG. **3** Panel C). Together, these data show the feasibility of protein co-expression in *Sulfolobus* using these vectors.

Operons often rearrange but maintain co-regulation of functionally and physically associated proteins (25). Such cases result in subunits of assemblies located at distil locations in the genome. The *Sulfolobus* thermosome subunits are an example of noncontiguous genes encoding proteins that assemble into a functional molecule (26). To evaluate our ability to co-express non-contiguous genes

from a synthetic polycistronic mRNA, an artificial polycistronic construct containing thermosome subunits alpha (Sso0282) and gamma (Sso3000) was constructed. PCR products from individually amplified/tagged genes were assembled into a single polycistronic expression construct using seamless cloning (Invitrogen) (27, 28). To ensure high-level expression of both subunits, a ribosomal binding site was inserted between the two open reading frames on the polycistronic construct. Thermosomes are among the most abundant constitutively expressed proteins in *Sulfolobus* and can account for nearly 5% of the total cellular protein (29). The abundant thermosome polypeptides migrate at similar rates and appear as a prominent doublet of protein bands in *Sulfolobus* crude extracts. Recombinant thermosome subunits alpha and gamma expressed from the synthetic polycistronic vector resulted in dramatically increased thermosome levels visualized by coomassie blue-stained SDS-PAGE (FIG. **3** Panel D, left). Immunoblots confirmed recombinant thermosome expression of both the alpha and gamma subunits (FIG. **3** Panel E, right). Both subunits were expressed at approximately equal levels that were much higher than the endogenous thermosome and therefore markedly greater than 5% of the total cell protein (29).

Native localization of overexpressed recombinant proteins in *Sulfolobus*. The *Sulfolobus* gene Sso0316 encodes and extracellular tetrameric iron superoxide dismutase (30, 31). An overexpression construct of Sso0316 was generated to investigate whether overexpressed recombinant proteins properly localized within cell or in this case, into the surrounding medium. As described above, superoxide dismutase was placed under the control of the 61-nucleotide minimal AraS promoter and fused to a carboxy-terminal FLAG epitope tag and transferred into the pSMY1 vector. Two intracellular genes encoding a DNA replication protein (Sso0771) and an RNA polymerase subunit (Sso0071) were likewise cloned and tagged as control proteins. Extracellular partitions of *Sulfolobus* cultures for these three constructs was evaluated after 72 hours of growth under inducing conditions. Cell-free media was collected from cultures and 90% saturating ammonium sulfate used to precipitate extracellular proteins. Extracellular precipitates of controls showed nearly equal amounts of precipitating protein but none recognized by the FLAG antibody (FIG. **4** Panel A). In sharp contrast, the media from cells carrying the Sso0316 expression constructs revealed a tightly controlled expression and extracellular accumulation of the recombinant superoxide dismutase (FIG. **4** Panel A). Notably, the SOD-FLAG protein was visible on the coomassie stained gel.

To ensure that protein overexpression in *Sulfolobus* did not cause protein accumulation in the media due to leakage or cell lysis, extracellular fractions from three cultures overexpressing different proteins were compared. Protein localization was compared between the extracellular superoxide dismutase (SOD, Sso0316) and the intracellular DNA polymerase subunit D (PolD, Sso0071) and cell division control protein 6 (cdc6, Sso0771) (FIG. **4**B). Induced cultures were portioned into cellular and extracellular fractions and immunoblots used to visualize recombinant proteins in crude culture fractions. Cdc6, PolD, and SOD were clearly evident in the intracellular partitions (FIG. **4**B, left panel). In marked contrast, the extracellular partitions from the same cultures show only detectable levels of SOD under inducing conditions (FIG. **4**B, right panel).

Membrane Localization of overexpressed genes in *Sulfolobus*. Subcellular localization of proteins is often intimately linked to proper function. To further assess the localization of recombinant proteins within *Sulfolobus* we constructed a series of constructs expressing the subunits of the flagellin and pilin membrane assembly genes (FIG. **5** Panel A). *Sulfolobus* flagellin proteins are known and contain integral membrane protein Fla? (Sso2315), an integral and extracellular protein FlaB (Sso2323), and the membrane-associated intracellular ATPase components FlaH and FlaI (Sso2318 and Sso2316) (32).

Production of Purification-Free and immobilized Enzyme products. The combination of polycictronic constructs and targeted localization can be combined to produce extracellular solutions with high-levels of desired enzymatic activities with minimal purification or without purification. The application of single and/or multiple simultaneous gene expression can produce post-translationally modified enzyme mixes accumulating in the media and that do not require purification. Either filtration or centrifugation of cells from these cultures yields active enzyme mixes. We have reduced this to practice with single enzyme production where only concentration of the extracellular media is sufficient to produce active enzyme preparations (FIGS. **4-6**). In addition, we have demonstrated the capability to target assembly of immobilized enzymes both integral and associated with host membranes for future applications. Such membrane targeting and assembly could be used for industrial applications to immobilize active heat/acid/detergent stable enzymes onto engineered organic and inorganic surfaces and/or immobilized membrane rafts to be applied to industrial processes.

Enzymatic saccharification and pre-treatment in the same dilute sulfuric acid and temperature conditions. Standard pretreatment conditions for lignocellulosic biomass use sulfuric acid concentrations of 0.275-0.8% (v/v) acid and a temperature of 121° C. or greater. Here we establish a pretreatment regimen compatible with *Sulfolobus* growth conditions with 0.025% (v/v) sulfuric acid and 80° C. and demonstrate that enzymatic saccharification of raw plant biomass is comparable to yields with the harsher treatments (FIG. **9**). Solutions of 10% (m/v) pulverized switchgrass were made up in *Sulfolobus* growth media with either 0.025% or 0.025% sulfuric acid. The pretreatments were either 121° C. for 60 minutes or 80° C. for 10 hours. Saccharification to xylobiose was quantified after a 15-hour reaction with the noted *Sulfolobus* enzymes at 80° C. Sugar yields are from standard (0.25%, 121° C.) and the low-temp/low-acid pretreatments conditions (0.025%, 80° C.) are comparable with *Sulfolobus* enzymes (FIG. **9**). These data reveal that pretreatment of lignocellulosic feedstocks in *Sulfolobus* growth conditions (80° C., and 0.025% sulfuric acid) is compatible with; 1) pretreatment, 2) enzymatic saccharification using heat/acid stable enzymes expressed in *Sulfolobus*, and 3) *Sulfolobus* cell growth.

Cellulase stability in detergents. Thermal and acid stable cellulase also have a high degree of stability in various detergents (FIG. **10**).

The biodiversity available for exploitation has been partly limited by the availability of genetically tractable model organisms to express and purify proteins. The development of genetic tools to complement well-established model organisms like *E. coli* and yeast systems holds promise to expand our understanding and application of extremophiles and extremophilic proteins for industrial, ecological, and energy applications.

EXAMPLE 2

Recombinant Acid/Heat Stable Proteases in *Sulfolobus solfataricus*

We have isolated active acid and heat stable extracellular protease from *Sulfolobus solfataricus*. The enzyme is an

active protease in the 0.025-0.25% v/v H_2SO_4 at 80° C. isolated from the extracellular fraction of active cell cultures (FIG. **9**). In some embodiments, the protease is fused to an epitope or other purification tags such as polyhistidine or FLAG among others targeted to the extracellular compartment as described herein. These enzymes can be produced recombinantly in Archaea as described herein.

While the present invention has been described with reference to the specific embodiments thereof, it should be understood by those skilled in the art that various changes may be made and equivalents may be substituted without departing from the true spirit and scope of the invention. In addition, many modifications may be made to adapt a particular situation, material, composition of matter, process, process step or steps, to the objective, spirit and scope of the present invention. All such modifications are intended to be within the scope of the claims appended hereto.

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cacctgggaa ttagagacct tgtggtagat 90

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Met Lys Leu Ile Glu Met Leu Lys Glu Ile Thr Gln Val Pro Gly Ile
1 5 10 15

Ser Gly Tyr Glu Glu Arg Val Arg Glu Lys Ile Ile Glu Trp
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<220> FEATURE:
<223> OTHER INFORMATION: synthetic amino acid sequence

<400> SEQUENCE: 23

Met Val Asp Trp Glu Leu Met Lys Lys Ile Ile Glu Ser Pro Gly Val
1 5 10 15

Ser Gly Tyr Glu His Leu Gly Ile Arg Asp Leu Val Val Asp
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<210> SEQ ID NO 24
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<400> SEQUENCE: 24

gaggtgagtc gga 13

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Ile Asn Pro Ser Tyr Pro Gln Ser Asn Val Ile Ser Ala Leu Pro Ser
35 40 45

Asn Thr Asn Ile Ile Leu Tyr Phe Phe Ile Pro Pro Lys Asn Leu Asn
50 55 60

Glu Leu Tyr Leu Ile Ala Gln Glu Val Ala Asn His Gln Ile Lys Pro
65 70 75 80

Leu Ser Asn Ala Gln Leu Val Ser Met Phe Ser Asn Gln Asp Lys Val
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Asn Glu Ser Ile Lys Tyr Leu Glu Ser Lys Gly Phe Thr Ile Ile Tyr
100 105 110

Arg Ser Pro Phe Glu Ile Met Ala Glu Ala Pro Val Ser Leu Val Ser
115 120 125

Ser Val Phe Glu Thr Ser Phe Val Leu Ala Lys Ser Thr Asn Gly Glu
130 135 140

Ile Tyr Tyr Lys Pro Ala Gly Asn Val Lys Ile Pro Ser Thr Leu Asn
145 150 155 160

Asn Leu Leu Ile Gly Gly Leu Thr Asn Phe Thr Asn Val Ser Leu Pro
165 170 175

Leu Ile Gln Leu Gly Lys Leu Glu Asn Gly Asn Leu Ile Pro Asn Lys
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Gln Ala Tyr Ser Ser Phe Val Tyr Thr Phe Gln Phe Ser Ala Thr Trp
195 200 205

Tyr Thr Pro Lys Val Ile Glu Gly Ala Tyr Asn Ile Thr Pro Leu Leu
210 215 220

Asn Ser Thr Ala Asp Lys Lys Val Thr Ile Ala Ile Ile Asp Ala Tyr
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Gly Asp Pro Glu Ile Tyr Gln Asp Val Asn Leu Phe Asp Ala Arg Phe
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Gly Leu Pro Pro Ile Asn Leu Thr Val Leu Pro Val Gly Pro Tyr His
260 265 270

Pro Glu Asn Gly Leu Phe Thr Gly Trp Phe Glu Glu Val Ala Leu Asp
275 280 285

Val Glu Ala Ala His Ala Ala Ala Pro Tyr Ser Asn Ile Leu Leu Val
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Val Ala Pro Ser Ala Thr Leu Glu Gly Leu Phe Ser Ala Ile Asp Val
305 310 315 320

Val Val Ser Glu Asp Leu Ala Gln Val Val Ser Met Ser Trp Gly Leu
325 330 335

Pro Gly Ile Leu Phe Gly Ala Ser Gly Phe Tyr Ala Val Phe Asn Gly
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Ile Ile Phe Pro Asn Tyr Pro Tyr Tyr Asp Tyr Tyr Phe Glu Leu Gly
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385                 390                 395                 400

Ser Pro Phe Val Thr Ala Val Gly Gly Thr Ser Leu Phe Ala Asn Ile
                405                 410                 415

Thr Ser Gly Tyr Ile Ser Thr Tyr Asn Ser Thr Gly Asn Phe Gly Ala
            420                 425                 430

Glu Ile Ala Trp Ser Val Asn Pro Leu Tyr Phe Gly Val Ile Gln Gly
        435                 440                 445

Gly Val Ser Ser Gly Gly Gly Tyr Ser Gln Leu Phe Pro Ala Pro Trp
    450                 455                 460

Tyr Gln Arg Tyr Val Thr His Ser Asn Tyr Arg Ala Ile Pro Asp Val
465                 470                 475                 480

Ala Ala Asp Ala Asn Pro Tyr Thr Gly Phe Thr Ile Tyr Ala Leu Gly
                485                 490                 495

Gln Glu Val Val Ile Gly Gly Thr Ser Leu Ser Ala Pro Leu Trp Ala
            500                 505                 510

Gly Ile Ile Ala Asp Ile Asp Gly Ile Ile Gly His Pro Leu Gly Leu
        515                 520                 525

Val Asn Pro Ile Leu Tyr Glu Ile Tyr Gln Asn Thr Thr Leu Tyr His
    530                 535                 540

Gln Ala Phe His Gln Ile Ser Leu Gly Tyr Asn Gly Tyr Tyr Tyr Ala
545                 550                 555                 560

Asn Ser Ser Tyr Asn Leu Val Thr Gly Leu Gly Ser Pro Asn Ala Gly
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Met Leu Gly Val Ile Ile Lys His Ser Leu Ser Lys Ser Leu Ala Ile
            580                 585                 590

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Asn Tyr Thr Ile Thr Pro Asn Asn Pro Pro Asn Leu Trp Glu Ile Val
            660                 665                 670

Val Asn Gly Ser Ser Asp Gln Phe Thr Gly Val Gly Thr Val Glu Val
        675                 680                 685

Asp Val Gly Glu Ser Ile Asn Ile Val Ser Pro Ile Pro Tyr Pro Tyr
    690                 695                 700

Ser Phe Pro Ile Pro Tyr Asn Ser Pro Phe Gly Ile Glu Ala Trp Ile
705                 710                 715                 720

Tyr Tyr Pro Asn Gly Thr Pro Val Val Asn Gln Ser Val Thr Ala Tyr
                725                 730                 735

Leu Val Ser Asn Asp Gly Lys Leu Leu Ala Ser Ile Pro Leu Thr Met
            740                 745                 750

Met Ala Pro Gly Leu Tyr Glu Gly Ser Tyr Ala Leu Leu Pro Pro Leu
        755                 760                 765

Pro Gln Gly Thr Tyr Leu Leu Ile Val Asn Asp Ser Tyr Gly Ser Ala
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Pro Ile Asn Asp Gly Phe Pro Ala Ala Ser Pro Gly Gln Asn Ile Thr
                805                 810                 815

Ile Ile Asp Glu Val Leu Thr Pro Glu Leu Thr Gly Leu Phe Thr Ser
            820                 825                 830

Asn Val Thr Ala Tyr Ile Tyr Asn Gln His Gly Asn Leu Ile Asp Gln
        835                 840                 845

Val Lys Leu Thr Pro Ala Pro Asp Glu Ile Gln Phe Gly Val Tyr Leu
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Leu Phe Phe Leu Tyr Tyr Ala Asn Phe Thr Ile Pro Phe Asp Ala Ser
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Pro Gly Phe Tyr Asn Val Val Ile Gln Ser Ile Ser Asn Thr Ser Thr
                885                 890                 895

Gly Leu Val Lys Ala Asp Phe Ile Thr Ser Phe Tyr Val Ser Pro Ala
            900                 905                 910

Asn Leu Thr Leu Asn Val Lys Val Asn Asn Val Val Tyr Glu Gly Glu
        915                 920                 925

Leu Leu Lys Ile Phe Ala Asn Ile Thr Tyr Pro Asn Gly Thr Pro Val
    930                 935                 940

Lys Tyr Gly Met Phe Thr Ala Thr Ile Leu Pro Thr Ser Leu Asn Tyr
945                 950                 955                 960

Glu Gln Leu Ile Ile Gly Phe Glu Ala Gly Ile Pro Leu Gln Tyr Asn
                965                 970                 975

Ser Thr Leu Gly Glu Trp Val Gly Ile Tyr Ser Ile Pro Ser Ile Phe
            980                 985                 990

Tyr Gly Ser Ile Phe Gln Gly Ser  Ser Val Tyr Ser Leu  Ala Gly Pro
        995                 1000                1005

Trp Asn  Val Ile Val Ser Gly  Val Ser Trp Asn Gly  Tyr Asn Leu
    1010                1015                1020

Tyr Ser  Thr Pro Ser Ser Phe  Asn Phe Val Asn Val  Met Pro Tyr
    1025                1030                1035

Thr Phe  Ile Asn Asn Ile Val  Val Ser Ser Lys Ser  Leu Asp Ser
    1040                1045                1050

Pro Leu  Leu Ser Lys Ile Asn  Ser Thr Thr Tyr Met  Leu Ser Asn
    1055                1060                1065

Val Lys  Ser Asn Asn Ile Thr  Ile Asn Gly Met Asn  Val Ile Leu
    1070                1075                1080

Ser Asn  Val Ile Ala Asn Thr  Val Thr Val Lys Asn  Ser Asn Ile
    1085                1090                1095

Met Ile  Thr Ser Ser Thr Ile  Asn Gln Leu Val Leu  Asp Asn Ser
    1100                1105                1110

Ser Val  Ser Ile Ile Gly Ser  Lys Ile Gly Gly Asp  Asn Ile Ala
    1115                1120                1125

Val Val  Ala Asn Asp Ser Asn  Val Thr Ile Val Ser  Ser Val Ile
    1130                1135                1140

Gln Asp  Ser Lys Tyr Ala Phe  Leu Gln Pro Asn Ser  Val Ile Ser
    1145                1150                1155

Leu Ser  Gly Val Asn Met Tyr  Asn Val Thr Ser Leu  Ser Ser Ile
    1160                1165                1170

Pro Ala  Pro Arg Ile Thr Tyr  Leu Ser Thr Thr Asn  Val Thr Thr
    1175                1180                1185
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Ser Lys  Glu Ser Ile Ile Val  Asn Ile Thr Gly Glu  Tyr Leu Arg
    1190                 1195                 1200

Leu Leu  Gly Val Ser Met Asn  Asn Lys Pro Val Gly  Tyr Ser Val
    1205                 1210                 1215

Ile Ser  Ser Ser Pro Ser Ser  Ile Ser Leu Ser Ile  Pro Phe Asn
    1220                 1225                 1230

Ala Ser  Gln Leu Ser Asp Gly  Gln Tyr Ile Phe Thr  Val Ser Ile
    1235                 1240                 1245

Ser Asp  Gly Leu Pro Tyr Asn  Leu Thr Phe Asn Leu  Leu Asn Asn
    1250                 1255                 1260

Tyr His  Leu Ile Ile Val Gln  Asp His Leu Lys Ala  Leu Gln Gly
    1265                 1270                 1275

Ser Val  Asn Leu Leu Thr Val  Ile Ala Ile Ile Ser  Leu Ile Ile
    1280                 1285                 1290

Ala Ile  Ile Ala Val Ala Leu  Leu Phe Val Phe Thr  Arg Arg Arg
    1295                 1300                 1305
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<210> SEQ ID NO 26
<211> LENGTH: 875
<212> TYPE: PRT
<213> ORGANISM: Sulfolobus solfataricus

<400> SEQUENCE: 26

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Met Arg Leu Leu Lys Ile Leu Leu Leu Ala Met Leu Ile Leu Pro Leu
1               5                  10                  15

Phe Ser Phe Phe Thr Leu Ser Ile Ser Leu Tyr Asp Gln Ile Gln Leu
            20                  25                  30

Pro Pro His Tyr Leu Phe Tyr Ile Ser Glu Asn Ala Thr Gln Gly Ser
        35                  40                  45

Gly Ile Asp Val Ile Phe Tyr Thr Ser Ser Pro Ile Thr Phe Met Ile
    50                  55                  60

Met Thr Pro Ser Gln Phe Tyr Gln Phe Asn Gln Thr Gly Ser Ser Gln
65                  70                  75                  80

Ser Ile Tyr Ser Ile Thr Thr Asn Ser Leu Ser Lys Phe Phe Pro Leu
                85                  90                  95

Ser Gly Gln Tyr Tyr Ile Val Phe Tyr Asn Asn Ile Ser Asn Asn Pro
            100                 105                 110

Val Thr Leu Asn Tyr Tyr Ile Leu Thr Arg Pro Leu Pro Thr Gly Ile
        115                 120                 125

Ala Asp Tyr Gly Leu Lys Ile Asn Asn Gly Val Ile Ser Pro Tyr Ile
    130                 135                 140

Glu Lys Ile Lys Ser Val Ile Gly Ala Val Glu Ile Asn Lys Leu Leu
145                 150                 155                 160

Ala Tyr Asn Ser Thr Pro Pro Ala Gly Val Ser Gln Tyr Ser Ala Ser
                165                 170                 175

Ile Gln Leu Asn Val Val Leu Gln Val Asn Thr Ile Gly Gly Ser Gln
            180                 185                 190

Gln Leu Trp Leu Gln Asn Val Ile Gln Ile Tyr Thr Asn Asn Asp Ser
        195                 200                 205

Tyr Ile Phe Leu Asp Asn Ile Trp Asn Phe Thr Gly Lys Ile Ser Ile
    210                 215                 220

Leu Ser Asn Ser Thr Val Lys Gly Asn Gly Ile Val Tyr Val Thr Asn
225                 230                 235                 240

Asn Gly Asn Asp Tyr Tyr Ala Tyr Gly Thr Asn Phe Ser Thr Leu Leu
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                245                 250                 255

Ile Pro Ser Leu Lys Tyr Leu Leu Ile Asn Thr Ser Tyr Thr Ser Gln
            260                 265                 270

Gly Pro Met Ile Ser Phe Gly Tyr Met Asn Gln Ser Gly Ser Pro Ile
        275                 280                 285

Trp Tyr Asp Asn Val Thr Ile Leu Ile Pro Asn Thr Leu Ser Ala Tyr
    290                 295                 300

Ile Leu Val Asp Gly Tyr Asn Phe Thr Ala Gly Gly Leu Ala Tyr Asp
305                 310                 315                 320

Ala Glu Leu Ile Leu Gly Gly Gly Gly Asn Gly Glu Phe Thr Phe Phe
                325                 330                 335

Asn Glu Ser Asn Val Glu Leu Ala Met Ile Tyr Gln Tyr Leu Asn Gly
            340                 345                 350

Thr Leu Ala Pro Pro Lys Phe Leu Phe Pro Phe Gly Leu Asp Thr Glu
        355                 360                 365

Glu Ser Ala Asp Asn Leu Tyr Ser Ile Ser Tyr Asn Gly Val Tyr Leu
    370                 375                 380

Val Ser Ser Gly Tyr Gln Val Ile Asn Asn Leu Asn Glu Asn Val Ser
385                 390                 395                 400

Gln Leu Arg Phe Asn Val Val Asn Tyr Thr Lys Ala Thr Asp Gln Asn
                405                 410                 415

Phe Pro Tyr Ile Phe Thr Ile Asn Val Ser Gly Gly Val Leu Pro Tyr
            420                 425                 430

Lys Leu Asn Val Thr Ile Ser Asn Ser Ser Gly Asn Glu Leu Ser Gly
        435                 440                 445

Tyr Thr Tyr Val Leu Phe Pro Ser Val Ser Thr Tyr Tyr Leu Phe Leu
    450                 455                 460

Ser Pro Leu Ser Pro Gly Asn Tyr Thr Val Lys Ile Lys Leu Thr Asp
465                 470                 475                 480

Phe Asn Gly Asn Ser Lys Ser Tyr Glu Phe Ser Leu Thr Ile Asn Pro
                485                 490                 495

Pro Leu Lys Val Gln Ile Leu Asn Val Thr Asn Tyr Ile Asp Leu Ala
            500                 505                 510

Leu Pro Tyr Phe Asn Phe Thr Ser Ile Ile Ser Gly Gly Thr Lys Pro
        515                 520                 525

Tyr Asn Ile Ile Ile Thr Ile Ser Asn Asp Ser Gly Ile Leu Ser Glu
    530                 535                 540

Thr Tyr Lys Ile Ile Asn Tyr Thr Ser Ile Thr Tyr Tyr Ala Val Asn
545                 550                 555                 560

Met Lys Gly Tyr Ser Ile Gly Lys Tyr Thr Ile Gln Ile Glu Val Glu
                565                 570                 575

Asp Tyr Ala Gly Ser Ile Asn Ile Ser Lys Tyr Asn Phe Thr Ile Asn
            580                 585                 590

Pro Asn Pro Tyr Ile Ser Thr Leu Ser Tyr Thr Ser Glu Thr Asp Lys
        595                 600                 605

Gly Leu Arg Glu Val Ile Lys Ala Ile Gly Lys Gly Gly Ser Gly Ser
    610                 615                 620

Leu Ile Tyr Tyr Trp Tyr Val Asn Asn Ser Leu Val Ser Ser Gly Ile
625                 630                 635                 640

Gly Asp Glu Leu Tyr Asn Phe Thr Pro Ser Asn Ile Gly Glu Tyr Asn
                645                 650                 655

Ile Thr Val Met Val Lys Asp Val Leu Gly Val Ser Ser Ala Lys Ser
            660                 665                 670
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Val Ile Ile Lys Val Asn Pro Asp Pro Val Val Glu Leu Ser Val Pro
        675                 680                 685

Lys Thr Thr Ile Asp Ser Gly Ala Glu Phe Pro Val Asn Ala Thr Val
    690                 695                 700

Ser Leu Gly Thr Pro Pro Tyr Tyr Ile Ser Trp Tyr Ile Asn Gly Ser
705                 710                 715                 720

Tyr Val Gly Asn Glu Ser Ile Lys Glu Leu Asn Leu Ser Ser Ile Gly
                725                 730                 735

Val Tyr Ile Ile Thr Val Thr Val Arg Asp Ser Ala Gly Tyr Ile Ile
            740                 745                 750

Asn Met Ser Lys Pro Val Leu Ile Val Pro Pro Pro Ser Leu Ser Val
        755                 760                 765

Lys Glu Gln Thr Gln Gly Asn Phe Ile Gln Tyr Asn Thr Ser Ile Ala
    770                 775                 780

Leu Ser Ala Ser Val Asn Gly Gly Thr Asp Pro Tyr Tyr Leu Ile Phe
785                 790                 795                 800

Leu Asn Gly Lys Leu Val Gly Asn Tyr Ser Ser Thr Thr Gln Leu Gln
                805                 810                 815

Phe Lys Leu Gln Asn Gly Glu Asn Asn Ile Thr Leu Ile Ala Lys Asp
            820                 825                 830

Leu Trp Gly Lys Thr Ala Val Lys Thr Leu Ile Val Asn Ser Gly Tyr
        835                 840                 845

Asn Tyr Val Gly Ile Gly Ile Ile Ala Gly Ile Ile Leu Ile Ile Val
    850                 855                 860

Ile Val Val Ile Leu Val Ile Ser Lys Arg Lys
865                 870                 875


<210> SEQ ID NO 27
<211> LENGTH: 606
<212> TYPE: PRT
<213> ORGANISM: Sulfolobus solfataricus

<400> SEQUENCE: 27

Met Glu Ser Lys Asn Val Ile Leu Lys Arg Val Met Leu Leu Leu Val
1               5                   10                  15

Leu Ile Leu Ser Thr Thr Thr Phe Leu Thr Ile Ile Ala Gln Ser Gln
            20                  25                  30

Ala Gln Tyr Tyr Tyr Ile Gln Thr Ser Ser Pro Gln Tyr Thr Ile Ile
        35                  40                  45

Pro Gly Ser Val Phe Val Glu Pro Leu Asn Ser Ser Gln Thr Leu Tyr
    50                  55                  60

Ile Ala Val Leu Leu Asn Phe Thr Asn Leu Ala Ser Leu Gln Ser Tyr
65                  70                  75                  80

Leu Asn Glu Ile Tyr Leu Ser Ala Pro Gln Phe His His Trp Leu Thr
                85                  90                  95

Pro Ser Gln Phe Arg Glu Tyr Tyr Tyr Pro Ser Arg Ser Tyr Val Asn
            100                 105                 110

Ser Leu Ile Lys Tyr Leu Glu Ser Tyr Asn Leu Gln Phe Leu Gly Asn
        115                 120                 125

Tyr Gly Leu Ile Leu Val Phe Ser Gly Thr Val Gly Asn Ile Glu Lys
    130                 135                 140

Ala Phe Asn Thr Tyr Ile Asn Val Tyr Tyr Tyr Pro Phe Lys Asn Leu
145                 150                 155                 160

Tyr Trp Phe Gly Leu Leu Gly Ile Lys Asn Ile Gly Pro Phe Tyr Tyr
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                165                 170                 175

Tyr Ser Asn Asn Val Thr Pro Ser Leu Pro Phe Asn Ile Gly Lys Tyr
            180                 185                 190

Val Leu Gly Val Val Gly Ile Asp Ser Leu Asp Pro Lys Val Val Asn
        195                 200                 205

Val Val Thr Gln Thr Trp His Leu Pro Met Val Lys Ala Gln Ser Gly
    210                 215                 220

Leu Val Ser Lys Ala Ile Ile Ser Pro Ile Thr Ile Glu Gln Tyr Phe
225                 230                 235                 240

Asn Phe Thr Leu Ala Tyr Glu Arg Gly Tyr Thr Gly Gly Gly Ser Asn
                245                 250                 255

Ile Ala Ile Glu Gly Val Pro Glu Ser Phe Val Asn Val Ser Asp Ile
            260                 265                 270

Tyr Ser Phe Trp Gln Leu Tyr Gly Ile Pro Arg Thr Gly His Leu Asn
        275                 280                 285

Val Ile Tyr Phe Gly Asn Val Thr Thr Gly Gly Gln Ser Gly Glu Asn
    290                 295                 300

Glu Leu Asp Ala Glu Trp Ser Gly Ala Phe Ala Pro Ala Ala Asn Val
305                 310                 315                 320

Thr Ile Val Phe Ser Asn Gly Tyr Val Gly Gly Pro Gln Leu Val Gly
                325                 330                 335

Asn Leu Leu Asn Tyr Tyr Tyr Glu Tyr Tyr Tyr Met Val Asn Tyr Leu
            340                 345                 350

Asn Pro Asn Val Ile Ser Ile Ser Val Thr Val Pro Glu Ser Phe Leu
        355                 360                 365

Ala Ala Tyr Tyr Pro Ala Met Leu Asp Met Ile His Asn Ile Met Leu
    370                 375                 380

Gln Ala Ala Ala Gln Gly Ile Ser Val Leu Ala Ala Ser Gly Asp Trp
385                 390                 395                 400

Gly Tyr Glu Ser Asp His Pro Pro Pro Asn Phe His Ile Gly Thr Tyr
                405                 410                 415

Asn Thr Ile Trp Tyr Pro Glu Ser Asp Pro Tyr Val Thr Ser Val Gly
            420                 425                 430

Gly Ile Phe Leu Asn Ala Ser Ser Asn Gly Ser Ile Val Glu Ile Ser
        435                 440                 445

Gly Trp Asp Tyr Ser Thr Gly Gly Asn Ser Val Val Tyr Pro Ala Gln
    450                 455                 460

Ile Tyr Glu Ile Thr Ser Leu Ile Pro Phe Thr Pro Val Ile Val Arg
465                 470                 475                 480

Thr Tyr Pro Asp Ile Ala Phe Val Ser Ala Gly Gly Tyr Asn Ile Pro
                485                 490                 495

Glu Phe Gly Phe Gly Leu Pro Leu Val Phe Gln Gly Gln Leu Phe Val
            500                 505                 510

Trp Tyr Gly Thr Ser Gly Ala Ala Pro Met Thr Ala Ala Met Val Ala
        515                 520                 525

Leu Ala Gly Thr Arg Leu Gly Ala Leu Asn Phe Ala Leu Tyr His Ile
    530                 535                 540

Ser Tyr Gln Gly Ile Ile Glu Ser Pro Leu Gly Asn Phe Val Gly Lys
545                 550                 555                 560

Val Ala Trp Ile Pro Ile Thr Ser Gly Asn Asn Pro Leu Pro Ala His
                565                 570                 575

Tyr Gly Trp Asn Tyr Val Thr Gly Pro Gly Thr Tyr Asn Ala Tyr Ala
            580                 585                 590
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Met Val Tyr Asp Leu Leu Leu Tyr Ser Gly Leu Ile Glu Ser
        595                 600                 605


<210> SEQ ID NO 28
<211> LENGTH: 570
<212> TYPE: PRT
<213> ORGANISM: Sulfolobus solfataricus

<400> SEQUENCE: 28

Met Gln Phe Arg Lys Thr Phe Leu Phe Leu Asn Ile His Phe Pro Tyr
1               5                   10                  15

Val Leu Arg Asn Thr Leu Leu Ile Leu Leu Leu Leu Leu Pro Thr Pro
            20                  25                  30

Leu Leu Ala Ile Ser Leu Pro Thr Gly Val Val Ala Tyr Asp Gly Pro
        35                  40                  45

Ile Phe Thr Asn Gln Val Leu Gly Tyr Val Asn Ile Thr Ser Leu Gln
    50                  55                  60

Ala Tyr Asn Ala Ser Gly Ser Lys Phe Gly Val Pro Pro Tyr Gly Ala
65                  70                  75                  80

Ser Leu Gln Leu Asn Val Met Leu Gln Val Asn Thr Ser Asn Glu Glu
                85                  90                  95

Tyr Tyr Phe Trp Leu Gln Asn Val Ala Asp Phe Ile Thr Asn Glu Ser
            100                 105                 110

Lys Met Phe Phe Ser Glu Asn Ile Trp Asn Ser Thr Thr Pro Leu Ala
        115                 120                 125

Gly Ile Asn Asn Val Ile Gly Lys Gly Glu Ile Tyr Ser Thr Ser Asp
    130                 135                 140

Leu Phe Ser His Ser Ser Tyr Tyr Ala Tyr Gly Thr Tyr Tyr Ile Lys
145                 150                 155                 160

Tyr Asp Phe Pro Phe Ser Phe Tyr Leu Ile Val Asn Glu Ser His Asn
                165                 170                 175

Asn Gln Gly Val Tyr Val Ser Phe Gly Tyr Val Ile Leu Gln Asn Gly
            180                 185                 190

Asn Ile Thr Pro Pro Asn Pro Thr Phe Tyr Asp Thr Val Phe Ile Pro
        195                 200                 205

Val Asn Asn Leu Thr Ser Ala Ser Ile Ile Ile Ala Asn Gln Thr Thr
    210                 215                 220

Pro Asn Leu Asn Leu Gly Ile Ile Thr Tyr Leu Gly Ser Tyr Leu Asp
225                 230                 235                 240

Ala Glu Leu Val Trp Gly Gly Phe Gly Asn Gly Ala Ser Thr Thr Phe
                245                 250                 255

Leu Asn Met Ser Ser Tyr Leu Ala Leu Leu Tyr Met Lys Asn Gly Lys
            260                 265                 270

Trp Val Pro Phe Ser Gln Val Tyr Asn Tyr Gly Ser Asp Thr Ala Glu
        275                 280                 285

Ser Thr Asn Asn Leu Arg Val Thr Ile Ala Lys Asn Gly Asp Ala Tyr
    290                 295                 300

Val Thr Ile Gly Lys Gln Asn Pro Gly Leu Leu Thr Thr Asn Phe Asn
305                 310                 315                 320

Pro Ser Ile Pro Gly Phe Leu Tyr Leu Asn Ile Ser Ser Lys Ile Pro
                325                 330                 335

Phe Leu Val Asn Asn Ile Ile Ser Arg Thr Phe Ser Gly Tyr Val Ser
            340                 345                 350

Ala Pro Ile Lys Leu Gly Phe Phe Met Asn Tyr Ser Ile Asn Ser Ser
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        355                 360                 365

Ser Phe Ala Val Leu Asn Gly Asn Tyr Pro Ser Leu Ile Glu Pro Asn
    370                 375                 380

Val Ser Trp Phe Lys Ile Leu Asn Ile Ile Pro Asn Tyr Thr Tyr Tyr
385                 390                 395                 400

Tyr Leu Val Arg Val Asn Ser Ser Ile Pro Val Ile Gly Thr Ile Asn
                405                 410                 415

Gly Lys Gln Ile Thr Leu Asn Asp Thr Asn Trp Phe Ala Gln Gly Thr
            420                 425                 430

Gln Ile Lys Ile Val Asn Tyr Thr Tyr Tyr Asn Gly Ser Asp Glu Arg
        435                 440                 445

Tyr Val Ile Ser Ser Ile Leu Pro Ser Leu Ser Phe Asn Ile Ser Ser
    450                 455                 460

Pro Leu Asn Val Thr Ile Asn Thr Ile Lys Gln Tyr Arg Val Ile Ile
465                 470                 475                 480

Asn Ser Asp Leu Pro Thr Tyr Leu Asn Asp Lys Arg Val Asn Gly Ser
                485                 490                 495

Ile Trp Ile Asn Thr Gly Thr Ile Val Lys Leu Ser Ala Ser Ile Pro
            500                 505                 510

Phe Tyr Glu Val Gly Arg Phe Ile Gly Thr Tyr Asn Leu Thr Leu Gly
        515                 520                 525

Gly Thr Ile Val Val Asn Lys Pro Ile Val Glu Lys Leu Gln Leu Ser
    530                 535                 540

Ile Asn Asn Leu Leu Leu Glu Ile Thr Ala Ile Ile Ile Val Ile Val
545                 550                 555                 560

Ile Ile Met Leu Ile Leu Arg Lys Arg Arg
                565                 570


<210> SEQ ID NO 29
<211> LENGTH: 556
<212> TYPE: PRT
<213> ORGANISM: Sulfolobus solfataricus

<400> SEQUENCE: 29

Met Leu Lys His Ile Val Leu Val Leu Leu Leu Leu Leu Thr Pro
1               5                   10                  15

Leu Val Ala Ile Ser Phe Pro Thr Gly Val Val Ala Tyr Asn Gly Pro
            20                  25                  30

Ile Cys Thr Asn Glu Val Leu Gly Tyr Ala Asn Ile Ser Ser Leu Leu
        35                  40                  45

Ala Tyr Asn Thr Ser Ala Ser Gln Leu Gly Val Pro Pro Tyr Gly Ala
    50                  55                  60

Ser Leu Gln Leu Asn Val Met Leu Glu Val Asn Thr Ser Gly Gly Glu
65                  70                  75                  80

Tyr Tyr Phe Trp Leu Gln Asn Val Ala Asp Phe Ile Thr Asn Glu Ser
                85                  90                  95

Lys Val Phe Phe Gly Asp Asn Ile Trp Asn Ser Thr Thr Pro Phe Ala
            100                 105                 110

Gly Ile Asn Asn Ile Val Gly Lys Gly Glu Ile Tyr Ser Thr Ser Asp
        115                 120                 125

Phe Phe Ser His Ser Ser Tyr Tyr Ala Tyr Gly Thr Tyr Tyr Ile Lys
    130                 135                 140

Tyr Asn Phe Pro Phe Ser Phe Tyr Leu Ile Ile Asn Glu Ser Tyr Asp
145                 150                 155                 160
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Thr Gln Gly Val Tyr Val Ser Phe Gly Tyr Val Ile Leu Gln Asn Gly
                165                 170                 175

Asn Ile Ser Pro Pro Asn Pro Ile Phe Tyr Asp Thr Val Phe Ile Pro
            180                 185                 190

Ile Gln Asn Leu Ser Phe Ala Ser Ile Ile Ile Ala Asn Gln Thr Thr
        195                 200                 205

Pro Ser Ala Asn Phe Gly Ile Val Thr Tyr Leu Gly Asn Tyr Leu Asp
    210                 215                 220

Ala Glu Leu Val Trp Gly Gly Phe Gly Asn Gly Glu Ser Thr Thr Phe
225                 230                 235                 240

Leu Asn Met Ser Ser Tyr Leu Ala Leu Leu Tyr Met Lys Ser Gly Glu
                245                 250                 255

Trp Val Pro Phe Ser Gln Val Tyr Asn Tyr Gly Ser Asp Thr Ala Glu
            260                 265                 270

Ser Thr Asn Asn Leu Gln Val Leu Ile Gly Lys Asn Gly Asp Ala Tyr
        275                 280                 285

Val Thr Ile Gly Arg Gln Asn Pro Gly Leu Leu Thr Thr Lys Phe Asn
    290                 295                 300

Pro Ser Tyr Pro Ser Phe Leu Tyr Leu Asn Ile Ser Ser Lys Ile Pro
305                 310                 315                 320

Phe Leu Leu Asn Lys Ser Leu Ser His Ala Phe Ser Gly Tyr Val Thr
                325                 330                 335

Thr Gln Ile Lys Leu Gly Phe Phe Lys Asn Tyr Ser Ile Asn Ser Ser
            340                 345                 350

Ser Phe Ala Val Leu Asn Gly Asn Tyr Pro Ser Leu Ile Glu Pro Asn
        355                 360                 365

Val Ser Trp Phe Lys Val Leu Asn Ile Ile Pro Asn Tyr Thr Tyr Tyr
    370                 375                 380

Tyr Leu Val Lys Val Asn Ser Gln Ile Pro Val Ile Ala Asn Val Asn
385                 390                 395                 400

Gly Lys Gln Ile Thr Leu Asn Ser Thr Asp Trp Phe Ala Gln Gly Thr
                405                 410                 415

Gln Ile Ser Ile Leu Asn Tyr Thr Tyr Tyr Asn Gly Ser Asn Glu Arg
            420                 425                 430

Tyr Ile Ile Ser Ser Ile Leu Pro Ser Ser Ser Phe Asn Val Ser Leu
        435                 440                 445

Pro Leu Asn Ile Thr Leu Ser Thr Ile Lys Gln Tyr Arg Val Leu Val
    450                 455                 460

Asp Ser Asn Leu Pro Val Tyr Leu Asn Gly Glu Arg Val Asn Gly Ser
465                 470                 475                 480

Val Trp Ile Asn Ala Gly Ser Ser Ile Gln Leu Ser Ala Asn Val Pro
                485                 490                 495

Phe Tyr Glu Lys Gly Ile Phe Thr Gly Thr Tyr Asn Val Thr Pro Gly
            500                 505                 510

Ser Ile Ile Thr Val Asn Gly Pro Ile Val Glu Thr Leu Ile Leu Ser
        515                 520                 525

Ile Asn Thr Glu Leu Met Gly Ile Val Ala Val Ile Val Ile Ala Val
    530                 535                 540

Val Ala Ile Ala Ile Leu Val Leu Arg Arg Arg Arg
545                 550                 555
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<210> SEQ ID NO 30
<211> LENGTH: 443
<212> TYPE: PRT

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<213> ORGANISM: Sulfolobus solfataricus

<400> SEQUENCE: 30

Met Met Tyr Lys Val Leu Leu Ile Ile Ile Leu Leu Leu Pro Leu Ser
1 5 10 15

Met Pro Leu Ser Ile Pro Thr Thr Ser Gln Pro Ser Ala Leu Ala Phe
20 25 30

Pro Ser Gly Val Thr Ser Tyr Pro Leu Asn Thr Ile Ile Tyr Thr Asp
35 40 45

Phe Val Met Gly Arg Ile Asn Ile Ser Tyr Leu Asn Ile Gly Ser Ser
50 55 60

Tyr Leu Pro Gly Gly Glu Tyr Phe Thr Thr Gly Asn Ala Ser Leu Gln
65 70 75 80

Leu Asn Ala Met Val Leu Gly Glu Tyr Trp Ala Gln Asn Val Ile Leu
85 90 95

Phe His Gln Ile Ser Asn Asn Thr Phe Tyr Ala Thr Leu Ile Val Asn
100 105 110

Leu Trp Asn Leu Ser Gly Pro Phe Ser Asn Thr Thr Ser Asn Ser Leu
115 120 125

Val Tyr Gln Gly Leu Gly Val Ile Cys Tyr Gln Gly Pro Thr Phe Lys
130 135 140

Val Thr Leu Pro Leu Ser Ile Ser Leu Phe Met Glu Ile Val Asn Ser
145 150 155 160

Thr Leu Asn Phe Gly Tyr Asn Ile Asn Gly Gln Lys Gly Ile Tyr Phe
165 170 175

Arg Tyr Pro Ile Ile Gly Leu Phe Gln Leu Gly Gly Leu Ser Leu Leu
180 185 190

Gly Leu Pro Asn Asp Leu Glu Leu Val Trp Gly Gly Pro Gly Gly Gly
195 200 205

Ser Val Val Phe Met Asn Val Ser Ser Ile Ala Asn Leu Tyr Tyr Phe
210 215 220

Asn Gly Asn Thr Leu Thr Ile Val Pro Asn Ala Tyr Ser Ile Gly Phe
225 230 235 240

Asp Thr Ala Glu Ser Ala Tyr Gly Val Lys Val Tyr Ser Thr Phe Pro
245 250 255

Ser Val Phe Ser Pro Ile Val Ile Glu Thr Ser Gly Val Asn Val Pro
260 265 270

Ser Val Leu Trp Pro Ile Pro Pro His Val Leu Val Asn Gln Thr Ser
275 280 285

Asn Lys Ile Thr Val Lys Leu Ser Ile Ser Asn Lys Ser Leu Ser Gly
290 295 300

Gln Ala Val Tyr Leu Glu Thr Gly Phe Pro Pro Ser Val Ile Ser Ser
305 310 315 320

Ala Val Thr Asn Ser Ser Gly Ile Ala Val Phe Pro Asn Asn Asn Tyr
325 330 335

Ser Phe Tyr Val Val Tyr Phe Pro Gly Asn Phe Thr Leu Ser Ser Thr
340 345 350

Tyr Tyr Phe Ser Ser Pro Ile Leu Asn Ser Leu Ser Ser Lys Phe Arg
355 360 365

Ser Tyr Tyr Gln Asp Leu Leu Asn Phe Leu Asn Ser Ala Gln Asn Ser
370 375 380

Phe Lys Lys Gly Ile Lys Ser Val Leu Ser Lys Gln Glu Thr Ser Ile
385 390 395 400

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Thr Thr Thr Thr Leu Thr Ser Thr Thr Ser Ser Ser Ser Gln Phe Gly
                405                 410                 415

Val Asn Leu Tyr Ile Val Leu Tyr Ile Leu Ala Phe Val Ile Gly Met
            420                 425                 430

Val Ile Ser Ala Ile Leu Ile Arg Phe Lys Leu
        435                 440


<210> SEQ ID NO 31
<211> LENGTH: 1077
<212> TYPE: PRT
<213> ORGANISM: Sulfolobus solfataricus

<400> SEQUENCE: 31

Met Thr Trp Ser Ile Phe Leu Leu Ile Leu Ala Leu Ser Asp Ile Val
1               5                   10                  15

Leu Pro Leu Thr Ile Thr Asn Ile Asn Asn Gln Ser Ile Thr Thr Leu
            20                  25                  30

Ser Pro Asn Tyr Tyr Leu Thr Val Ala Ile Val Phe Pro Pro Ser Asn
        35                  40                  45

Leu Thr Leu Leu Gln Gln Tyr Val Gln Glu His Val Ile Leu Asn Gln
    50                  55                  60

Thr Gln Val Glu Lys Leu Phe Ile Pro Thr Glu Glu Ile Ser Lys Thr
65                  70                  75                  80

Leu Ser Gln Leu Arg Gln Ser Asn Ile Ser Ala Thr Ser Tyr Met Asn
                85                  90                  95

Val Ile Leu Ala Ser Gly Thr Val Ser Gln Leu Glu Lys Ala Leu Asn
            100                 105                 110

Gly Lys Phe Tyr Val Tyr Glu Leu Asn Gly Lys Arg Phe Phe Glu Phe
        115                 120                 125

Phe Gly Ser Pro Val Ile Pro Asn Ala Ile Val Ile Gly Thr Asn Ile
    130                 135                 140

Thr Ser Leu Ile Leu Asn Lys Pro Thr Thr Leu Tyr Asn Val Thr Gln
145                 150                 155                 160

Ala Val Ala Tyr Asn Ala Leu Lys Pro Ser Gln Leu Leu Tyr Ala Tyr
                165                 170                 175

Asn Ile Ser Trp Leu His Ala His Asn Ile Thr Gly Lys Gly Thr Ala
            180                 185                 190

Ile Gly Ile Leu Asp Phe Tyr Gly Asn Pro Tyr Ile Gln Gln Gln Leu
        195                 200                 205

Gln Glu Phe Asp Lys Gln Tyr Asn Ile Pro Asn Pro Pro Phe Phe Lys
    210                 215                 220

Ile Val Pro Ile Gly Ala Tyr Asn Pro Asn Asn Gly Ile Ser Thr Gly
225                 230                 235                 240

Trp Ala Met Glu Ile Ser Leu Asp Val Glu Tyr Ala His Val Ile Ala
                245                 250                 255

Pro Asp Ala Gly Ile Val Leu Tyr Val Ala Asn Pro Asn Ile Pro Leu
            260                 265                 270

Pro Ala Ile Ile Ala Tyr Ile Val Gln Gln Asp Glu Val Asn Val Val
        275                 280                 285

Ser Gln Ser Phe Gly Ile Pro Glu Leu Tyr Val Asp Leu Gly Leu Ile
    290                 295                 300

Pro Leu Ser Tyr Val Asn Ser Leu Met Tyr Glu Tyr Trp Leu Gly Glu
305                 310                 315                 320

Val Glu Gly Ile Ser Phe Ala Ala Ala Ser Gly Asp Ala Gly Gly Asn
                325                 330                 335
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Gly Tyr Asn Tyr Phe Leu Ala Pro Gln Gly Ser Val Ile Phe Pro Ala
            340                 345                 350

Ser Ile Pro Tyr Val Leu Ala Val Gly Gly Ser Ser Val Tyr Ile Gly
        355                 360                 365

Gly Asn Lys Thr Met Glu Thr Ala Trp Ser Gly Glu Ser Val Leu Gly
    370                 375                 380

Ala Ser Thr Gly Gly Tyr Ser Thr Leu Phe Pro Ala Pro Trp Tyr Gln
385                 390                 395                 400

Asp Ser Asn Gly Phe Arg Val Val Pro Asp Val Val Ala Asp Ala Asn
                405                 410                 415

Pro Tyr Thr Gly Ala Phe Ile Leu Tyr Tyr Tyr Asn Gln Thr Tyr Leu
            420                 425                 430

Val Gly Gly Thr Ser Leu Ala Thr Pro Ile Val Ser Gly Ile Ile Asp
        435                 440                 445

Leu Met Thr Gln Ser Tyr Gly Lys Leu Gly Phe Val Asn Pro Phe Leu
    450                 455                 460

Tyr Glu Leu Arg Asn Thr Ser Ala Leu Ser Pro Ile Gly Phe Gly Tyr
465                 470                 475                 480

Asn Thr Pro Tyr Tyr Val Asn Ser Ser Glu Leu Asn Pro Val Thr Gly
                485                 490                 495

Leu Gly Ser Ile Asn Ala Gly Tyr Leu Tyr Gln Leu Leu Pro Lys Val
            500                 505                 510

Ile His Ser Ser Ser Ile Ser Val Gly Val Asn Asn Ile Thr Tyr Leu
        515                 520                 525

Asp Gly Gln Val Val Lys Val Val Ala Asn Ile Thr Gly Ile Arg Pro
    530                 535                 540

Ser Ser Val Ile Gly Ile Val Tyr Asn Gly Ser Ser Val Val Gln Gln
545                 550                 555                 560

Phe Ser Leu Ser Phe Asn Gly Thr Tyr Trp Val Gly Glu Phe Val Ala
                565                 570                 575

Glu Gly Ser Gly Ile Glu Glu Val Ile Val Lys Ala Gly Asn Leu Glu
            580                 585                 590

Gly Ser Thr Tyr Val Thr Ile Gly Tyr Gln Ala Gln Phe Ile Phe Pro
        595                 600                 605

Pro Ile Ala Leu Phe Pro Glu Pro Glu Pro Val Pro Ile Val Val Gln
    610                 615                 620

Leu Ile Tyr Pro Asn Gly Ser Leu Val Arg Asn Pro Ser Asn Leu Thr
625                 630                 635                 640

Ala Leu Ile Tyr Lys Tyr Asp Gln Met Asn Asn Lys Met Ser Ile Ile
                645                 650                 655

Ser Ser Val Gln Leu Gln Arg Thr Ser Leu Ile Asn Leu Ser Ile Leu
            660                 665                 670

Gly Ile Gln Ile Glu Ser Ser Tyr Leu Thr Gly Val Tyr Gln Leu Pro
        675                 680                 685

Ser Asn Ile Ile Ser Gly Val Tyr Phe Ile Lys Ile Pro Asn Val Phe
    690                 695                 700

Gly Phe Asp Glu Phe Val Ser Gly Ile Tyr Ile Leu Asp Ala Val Tyr
705                 710                 715                 720

Pro Pro Val Phe Thr Asn Pro Val Val Leu Ser Pro Gly Gln Asn Val
                725                 730                 735

Thr Ile Leu Ala Glu Ala Leu Ala Ile Gly Ser Pro Asn Val Thr Val
            740                 745                 750
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Thr Phe Tyr Asn Ile Ser Gly Asn Lys Val Tyr Ser Ile Pro Val Asn
        755                 760                 765

Ala Ile Thr Tyr Gln Asn Thr Leu Leu Tyr Ile Thr Gln Ile Thr Leu
    770                 775                 780

Pro Lys Leu Lys Pro Gly Tyr Tyr Tyr Val Val Thr Lys Ala Ile Tyr
785                 790                 795                 800

Asn Ala Ser Asn Phe Thr Ala Glu Gly Val Gly Leu Thr Gln Ile Tyr
                805                 810                 815

Val Ser Pro Tyr Ser Leu Asn Val Lys Val Arg Ile Ile Pro Asn Asn
            820                 825                 830

Ser Ile Val Tyr Gln Asn Gln Gln Ile Tyr Val Ile Ala Asn Ile Thr
        835                 840                 845

Tyr Pro Asn Gly Thr Glu Val Lys Tyr Gly Ser Phe Ser Ala Ile Ile
    850                 855                 860

Val Pro Ser Tyr Leu Ser Ser Gln Phe Asp Asn Leu Gln Leu Gln Tyr
865                 870                 875                 880

Ser Val Pro Leu Thr Tyr Ile Asn Gly Ser Trp Ile Gly Gln Leu Glu
                885                 890                 895

Ile Pro Ser Gly Ser Ser Thr Asn Ser Leu Gly Tyr Ser Thr Tyr Gly
            900                 905                 910

Ile Ser Gly Tyr Trp Asp Val Tyr Val Glu Gly Ile Ser Ala Asp Gly
        915                 920                 925

Ile Pro Thr Asn Phe Pro Ala Thr Leu Asp Val Asn Thr Leu Ser Ile
    930                 935                 940

Asn Pro Ile Ser Pro Ser Ser Gln Phe Val Val Leu Pro Tyr Val Tyr
945                 950                 955                 960

Val Ser Val Phe Asn Gly Thr Ile Ala Phe Asn Glu Phe Ile Asp Lys
                965                 970                 975

Ala Ile Val Val Gly His Asn Ala Thr Phe Ile Asn Ser Ile Ile Arg
            980                 985                 990

Asn Leu Ile Val Glu Asn Gly Thr  Val Thr Leu Ile Asn  Ser Lys Val
        995                 1000                1005

Gln Asn  Val Ser Leu Val Asn  Ser Glu Ile Ile Lys  Ile Asn Ser
    1010                1015                1020

Thr Val  Gly Asn Asn Val Asn  Tyr Ile Thr Thr Ile  Gly Asn Asn
    1025                1030                1035

His Ala  Lys Ser Ser Tyr Pro  Ser Leu Asp Ser Gly  Ser Ile Leu
    1040                1045                1050

Thr Ile  Gly Ile Val Leu Asp  Ile Ile Thr Ile Ile  Ala Leu Ile
    1055                1060                1065

Leu Ile  Lys Arg Arg Lys Lys  Phe Ile
    1070                1075


<210> SEQ ID NO 32
<211> LENGTH: 141
<212> TYPE: PRT
<213> ORGANISM: Sulfolobus solfataricus

<400> SEQUENCE: 32

Met Lys Met Lys Lys Ser Asp Ile Ile Ile Ile Leu Phe Ile Ala Leu
1               5                   10                  15

Ile Tyr Ile Leu Met Phe Ser Asn Ile Val Gln Ser Ala Ser Val Glu
            20                  25                  30

Gly Val Ser Met Tyr Pro Ile Phe Gln Asn Gly Ala Leu Thr Phe Tyr
        35                  40                  45
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Val Lys Pro Ile Ser Ile Asn Glu Gly Asn Val Ile Ile Tyr Lys Ser
50 55 60

Pro Tyr Phe Asn Asn Tyr Val Ile His Arg Val Ile Ala Thr Asp Asn
65 70 75 80

Gly Tyr Tyr Ile Thr Gln Gly Val Asp Lys Ile Thr Asn Pro Ile Pro
85 90 95

Asp Asn Arg Ile Gly Leu Glu Pro Ala Ser Gly Ile Pro Lys Asn Leu
100 105 110

Val Val Gly Lys Ile Val Glu Phe Gly Asn Phe Thr Phe Ser Ile Pro
115 120 125

Tyr Leu Gly Tyr Ile Ser Ile Leu Phe Ser Ser Ile Ile
130 135 140

<210> SEQ ID NO 33
<211> LENGTH: 1269
<212> TYPE: PRT
<213> ORGANISM: Sulfolobus solfataricus

<400> SEQUENCE: 33

Met Tyr Arg Tyr Ile Phe Leu Met Ser Met Leu Leu Ile Ser Ile Ile
1 5 10 15

Pro Leu Val Phe Ala Ser Asn Pro Asn Met Tyr Gln Asn Pro Ile Thr
20 25 30

Leu Lys Glu Phe Arg Glu Ile Gly Thr Leu Asn Ala Asn Glu Glu Val
35 40 45

Ile Val Thr Ile Phe Val Pro Leu Lys Asn Leu Asp Leu Leu Tyr Tyr
50 55 60

Tyr Ala Ser Gly Ala Ser Asn Pro Ala Ser Pro Leu Tyr His Lys Phe
65 70 75 80

Leu Ser Pro His Glu Val Gln Gln Leu Phe Leu Pro Thr Glu Glu Tyr
85 90 95

Asn Gln Ile Leu Asn Tyr Val Lys Ser Ser Gly Phe Gln Val Ile Phe
100 105 110

Thr Ala Ser Asn Ser Val Ile Val Ile Lys Gly Thr Val Gly Gln Val
115 120 125

Glu Lys Tyr Leu Gly Thr Lys Tyr Ala Val Tyr Ser Asn Gly Ser Val
130 135 140

Thr Tyr Tyr Thr Asn Tyr Gly Tyr Pro Lys Ile Asn Ala Tyr Val Tyr
145 150 155 160

Ser Ser Asn Ile Ser Ala Ile Phe Phe Ala His Pro Ser Thr Leu Ile
165 170 175

Thr Glu Ser Thr Ile Lys Ser Phe Gln Gln Glu Ile Asn Gln Thr Phe
180 185 190

Pro Leu Glu Gly Tyr Trp Pro Thr Val Leu Gln Lys Val Tyr Asn Val
195 200 205

Thr Thr Glu Gly Glu Asn Thr Thr Ile Gly Ile Leu Asp Phe Tyr Gly
210 215 220

Asp Pro Tyr Ile Val Gln Gln Leu Ala Tyr Phe Asp Lys Ile Thr Gly
225 230 235 240

Leu Pro Asn Pro Pro Asn Phe Ser Val Val Pro Ile Gly Pro Tyr Asn
245 250 255

Pro Asn Leu Gly Ile Val Thr Gly Trp Ala Gly Glu Ile Ser Leu Asp
260 265 270

Val Glu Val Ala His Ala Ile Ala Pro Lys Ala Asn Ile Thr Leu Tyr

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        275                 280                 285

Ile Ala Asn Pro Asn Ile Pro Leu Pro Ala Ile Ile Ala Tyr Ile Thr
    290                 295                 300

Ser Gln Asn Lys Val Asp Thr Leu Ser Gln Ser Phe Ser Ile Pro Glu
305                 310                 315                 320

Ser Leu Phe Ser Ser Leu Phe Asn Gly Pro Leu Phe Tyr Ser Cys Ile
                325                 330                 335

Ile Leu Ser Asp Glu Tyr Tyr Ala Leu Gly Ser Ala Glu Gly Ile Thr
            340                 345                 350

Phe Leu Ala Ser Ser Gly Asp Ala Gly Gly Ser Gly Tyr Ser Asn Gly
        355                 360                 365

Pro Ile Gly Thr Val Gly Tyr Pro Ser Thr Ser Pro Phe Val Thr Ser
    370                 375                 380

Val Gly Gly Thr Thr Val Tyr Val Gln Phe Pro Asn Gly Ser Tyr Tyr
385                 390                 395                 400

Gln Thr Ala Trp Ser Asn Tyr Gly Phe Val Pro Asn Asn Val Asn Tyr
                405                 410                 415

Gly Gly Ser Thr Gly Gly Val Ser Ile Ile Glu Pro Lys Pro Trp Tyr
            420                 425                 430

Gln Trp Gly Leu Pro Thr Pro Ser Thr Tyr Pro Asn Gly Lys Leu Ile
        435                 440                 445

Pro Glu Ile Ser Ala Asn Ala Asn Val Tyr Pro Gly Ile Tyr Ile Val
    450                 455                 460

Leu Pro Ser Asn Thr Thr Gly Ile Thr Gly Gly Thr Ser Glu Ala Ser
465                 470                 475                 480

Pro Leu Thr Ala Gly Val Leu Ala Thr Ile Glu Ser Tyr Thr His His
                485                 490                 495

Arg Ile Gly Leu Leu Asn Pro Ile Leu Thr Tyr Met Ala Glu Asn Tyr
            500                 505                 510

Tyr Gly Lys Val Ile Glu Pro Ile Thr Phe Gly Tyr Asn Ile Pro Trp
        515                 520                 525

Val Ala Thr Tyr Gly Tyr Asn Leu Val Thr Gly Tyr Gly Thr Ile Asn
    530                 535                 540

Ala Gly Tyr Phe Glu Lys Ile Leu Pro Thr Leu Asn Leu Ser Lys Glu
545                 550                 555                 560

Leu Asn Val Ile Val Ser Val Tyr Asn Thr Ser Ile Pro Thr Val Ser
                565                 570                 575

Pro Gln Gln Phe Tyr Pro Gly Gln Arg Ile Leu Val Thr Ala Asn Ile
            580                 585                 590

Thr Tyr Pro Asn Gly Ser Pro Val Gln Thr Gly Glu Phe Lys Ala Leu
        595                 600                 605

Ile Glu Asn Tyr Leu Gly Asn Leu Thr Thr Phe Asn Leu Thr Tyr Asn
    610                 615                 620

Ser Leu Thr Lys Leu Trp Thr Gly Ser Gly Val Leu Ser Asn Lys Ala
625                 630                 635                 640

Ser Gly Ile Leu Phe Val Tyr Val Tyr Gly Ser Ser Asp Gly Leu Arg
                645                 650                 655

Gly Ile Gly Tyr Tyr Glu Thr Phe Ser Gly Tyr Tyr Ile Thr Phe Asn
            660                 665                 670

Tyr Thr Thr Thr Phe Thr Pro Val Tyr Val Glu Leu Gly Asn Ala Glu
        675                 680                 685

Leu Gly Ile Thr Leu Ser Asn Ser Tyr Phe Gln Ala Pro Ile Gly Val
    690                 695                 700
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Met Asn Ile Thr Leu Asn Ile Tyr Ser Tyr Asn Ile Thr Thr Asn Ala
705                 710                 715                 720

Tyr Thr Phe Val Thr Thr Leu Ser Val Pro Ile Lys Asn Gly Val Gly
                725                 730                 735

Val Ile Asp Leu Pro Pro Asp Leu Ser Ile Gly Asp Leu Leu Ile Ile
            740                 745                 750

Ala Glu Gly Asn Ala Tyr Gly Phe Asp Ala Phe Thr Asn Gly Val Tyr
        755                 760                 765

Met Gln Thr Leu Phe Ile Leu Pro Gln Val Val Val Glu Pro Gly Ser
    770                 775                 780

Val Ser Pro Gly Gln His Ile Thr Ile Glu Gly Ser Ile Ile Pro Pro
785                 790                 795                 800

Val Asn Leu Pro Ser Thr Thr Phe Gln Asp Ala Leu Gln Gly Thr Asn
                805                 810                 815

Ile Thr Ala Lys Leu Val Ser Ser Asn Gly Val Val Ile Asn Glu Ala
            820                 825                 830

Asn Ile Pro Leu Ser Pro Asn Gly Ile Tyr Phe Gly Tyr Leu Tyr Ile
        835                 840                 845

Pro Lys Asn Thr Pro Ser Gly Leu Tyr Asn Val Leu Leu Phe Ala Thr
    850                 855                 860

Tyr Tyr Ser Tyr Thr Leu Asn Thr Thr Ile Arg Gly Phe Tyr Tyr Gly
865                 870                 875                 880

Gln Ile Tyr Val Ser Asn Gln Ala Thr Ile Ser Val Lys Ser Val Asn
                885                 890                 895

Tyr Ala Phe Glu Gly Gln Thr Val Phe Ile Tyr Ala Asn Ile Thr Asn
            900                 905                 910

Gly Thr Asn Glu Ile Lys Phe Gly Met Phe Ser Ala Thr Val Tyr Pro
        915                 920                 925

Ser Ser Leu Ser Phe Asn Tyr Thr Thr Ile Ser Ser Ile Ile Glu Ile
    930                 935                 940

Pro Leu Trp Tyr Asn Pro Lys Ile Gly Glu Trp Glu Gly Asn Phe Thr
945                 950                 955                 960

Leu Pro Ser Ala Ile Ser Ala Gly Asn Leu Thr Tyr Leu Ala Gly Gln
                965                 970                 975

Gly Tyr Phe Gly Val Pro Phe Lys Val Leu Ile Thr Gly Ile Ser Ala
            980                 985                 990

Leu Gly Asn Pro Thr Thr Thr Asn  Ser Gly Asn Ala Tyr  Thr Ile Asn
        995                 1000                1005

Val Leu  Pro Tyr Thr Leu Phe  Thr Asn Gln Thr Leu  Asp Lys Thr
    1010                1015                1020

Leu Pro  Ser Tyr Ala Ser Leu  Val Asn Val Lys Ile  Leu Asn Val
    1025                1030                1035

Ser Gly  Asn Leu Leu Asn Asp  Phe Leu Thr Asn Val  Ile Ile Val
    1040                1045                1050

Asn Ser  Asn Val Lys Ile Leu  Asn Gly Asn Ile Ser  Asn Ile Val
    1055                1060                1065

Ile Arg  Asn Ser Thr Val Leu  Ile Met Gln Ser Asn  Ala Asn Asn
    1070                1075                1080

Ile Thr  Leu Tyr Asn Ser Thr  Leu Tyr Ala Ile Gly  Gly Ser Ile
    1085                1090                1095

Asn Gly  Leu Asn Val Val Asn  Ser Lys Val Val Pro  Ile Asn Ile
    1100                1105                1110
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His Ile  Gln Gly Leu Tyr Pro  Glu Leu Pro Ser Ile  Ser Ile Asn
    1115                1120                1125

Leu Pro  Ser Lys Asn Val Thr  Gly Thr Val Asn Val  Thr Val Asn
    1130                1135                1140

Val Ile  Gly Glu Asp Val Ser  Arg Ile Asn Val Tyr  Leu Asn Gly
    1145                1150                1155

Asn Leu  Ile Asn Ser Phe Thr  Thr Asn Gly Thr His  Ile Val Thr
    1160                1165                1170

Ile Asn  Thr Gln Asn Tyr Pro  Asp Gly Gly Tyr Asn  Leu Thr Val
    1175                1180                1185

Thr Ala  Ile Gln Ser Asp Gly  Leu Ser Ser Ser Asn  Ser Ser Tyr
    1190                1195                1200

Leu Tyr  Phe Glu Asn Gly Leu  Thr Asn Leu Asn Thr  Lys Val Asn
    1205                1210                1215

Val Ile  Ser Asn Gln Leu Thr  Asn Val Ser Asn Ser  Leu Ser Ser
    1220                1225                1230

Ser Ile  Ser Ser Leu Arg Thr  Ala Ser Leu Glu Tyr  Gln Ser Ile
    1235                1240                1245

Ser Leu  Ala Ile Gly Ile Ile  Ala Ile Val Leu Ala  Ile Leu Ala
    1250                1255                1260

Leu Val  Arg Arg Arg Arg
    1265
```

<210> SEQ ID NO 34
<211> LENGTH: 601
<212> TYPE: PRT
<213> ORGANISM: Sulfolobus solfataricus

<400> SEQUENCE: 34

```
Met Tyr Met Lys Ala Lys His Leu Ile Ser Leu Ile Val Ile Leu Thr
1               5                   10                  15

Pro Leu Val Thr Leu Leu Thr Ser Ala Val Tyr Thr Ser Gly Gly Ile
            20                  25                  30

Thr Phe Tyr Ser Pro Ala Tyr Asn Gly Glu Ser Tyr Tyr Thr Gly Gln
        35                  40                  45

Ser Ile Thr Ile Asp Ala Leu Leu Pro Gln Gln Phe Ala Thr Asp Ala
    50                  55                  60

Ala Thr Ile Asn Phe Phe Phe Pro Asn Ser Ser Leu Ala Val Thr Ile
65                  70                  75                  80

Pro Val Gln Ile Asn Gly Ser Gly Gly Ile Tyr Val Pro Asn Ala Tyr
                85                  90                  95

Ala Phe Pro Asn Val Pro Gly Thr Trp Gln Ile Thr Ile Glu Val Ala
            100                 105                 110

Gly Gly Val Ala Val Gly Thr Ile Asn Val Asn Val Ile Gln Arg Thr
        115                 120                 125

Pro Leu Val Thr Val His Leu Gly Tyr Gly Val Val Gly Gln Ala Leu
    130                 135                 140

Pro Gln Thr Pro Thr Ile Thr Leu Thr Phe Pro Asn Gly Thr Thr Ile
145                 150                 155                 160

Thr Val Pro Leu Gln Gly Thr Val Asn Val Pro Ser Gly Thr Ser Tyr
                165                 170                 175

Gln Val Glu Gln Ala Ile Thr Glu Asn Asn Ile Arg Trp Ala Thr Asn
            180                 185                 190

Tyr Thr Ser Gly Thr Ile Thr Pro Ala Thr Thr Ser Ile Thr Pro Thr
        195                 200                 205
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Tyr Tyr Gln Gln Tyr Leu Val Thr Phe Asn Tyr Thr Val Gln Gly Gly
    210                 215                 220

Thr Gly Tyr Ser Pro Pro Thr Val Tyr Tyr Arg Ser Leu Gly Met Asn
225                 230                 235                 240

Glu Thr Ala Lys Ala Pro Ala Ser Val Trp Val Asp Ala Asn Ser Ala
                245                 250                 255

Tyr Ile Tyr Ser Pro Glu Leu Gln Ser Asn Val Gln Gly Glu Arg Trp
            260                 265                 270

Ile Ala Val Asn Phe Thr Gly Ile Ile Lys Ala Pro Gly Glu Ile Asn
        275                 280                 285

Glu Tyr Tyr Ile Asn Gln Tyr Leu Val Thr Val Gln Ser Gln Ile Pro
    290                 295                 300

Val Tyr Ala Ile Val Asn Gly Ala Asn Glu Thr Leu Asn Ser Thr Asn
305                 310                 315                 320

Trp Phe Thr Gln Gly Thr Thr Ile Lys Leu Glu Asn Ile Thr Lys Tyr
                325                 330                 335

Val Ser Ser Val Glu Arg Tyr Val Ile Ala Asn Phe Ser Pro Ser Glu
            340                 345                 350

Val Ile Thr Val Asn Gln Pro Thr Thr Ile Lys Val Asn Thr Val Thr
        355                 360                 365

Gln Tyr Phe Ile Asn Val Asn Ser Pro Val Gln Leu Lys Ala Leu Ile
    370                 375                 380

Asn Gly Ala Asn Glu Ser Leu Thr Ala Gly Trp Tyr Asn Gln Gly Thr
385                 390                 395                 400

Ser Ile Lys Ile Glu Asn Leu Thr Tyr Tyr Val Gly Asn Gly Glu Arg
                405                 410                 415

Leu Ile Leu Gly Lys Val Leu Pro Ser Leu Glu Ile Ile Val Asn Gly
            420                 425                 430

Ser Tyr Thr Ile Ser Thr Thr Thr Ile Thr Gln Tyr Phe Val Asn Val
        435                 440                 445

Ser Ser Pro Ile Pro Val Gln Val Leu Ile Asn Gly Ser Lys Thr Ile
    450                 455                 460

Leu Asn Ser Ser Trp Ile Asn Ala Gly Thr Ser Ile Leu Val Leu Asn
465                 470                 475                 480

Tyr Thr Tyr Asn Ile Ser Pro Gln Glu Arg Val Ile Ile Val Gly Ile
                485                 490                 495

Ser Pro Ser Gln Ser Phe Thr Val Asn Ser Pro Glu Thr Leu Lys Leu
            500                 505                 510

Leu Thr Val Thr Gln Tyr Leu Val Thr Ile Asn Gly Val Ser Lys Phe
        515                 520                 525

Tyr Asn Ser Gly Ser Lys Ile Val Leu Asn Ala Ser Val Pro Phe Tyr
    530                 535                 540

Glu Thr Ala Thr Phe Lys Gly Thr Tyr Asn Val Ser Pro Gly Ala Thr
545                 550                 555                 560

Ile Thr Val Asn Gln Pro Ile Thr Glu Thr Leu Val Glu Ser Pro Asn
                565                 570                 575

Tyr Leu Ile Leu Gly Ala Ile Ala Ala Val Ile Ile Ile Val Val Ala
            580                 585                 590

Val Val Val Ile Ile Leu Leu Arg Arg
        595                 600
```

<210> SEQ ID NO 35
<211> LENGTH: 340

-continued

<212> TYPE: PRT
<213> ORGANISM: Sulfolobus acidocaldarius

<400> SEQUENCE: 35

Met Asn Phe Lys Ser Ile Cys Leu Ile Ile Leu Leu Ser Ala Leu Ile
1 5 10 15

Ile Pro Tyr Ile Pro Gln Asn Ile Tyr Phe Phe Pro His Arg Asn Thr
20 25 30

Thr Gly Ala Thr Ile Ser Ser Gly Leu Tyr Val Asn Pro Tyr Leu Tyr
35 40 45

Tyr Thr Ser Pro Pro Ala Pro Ala Gly Ile Ala Ser Phe Gly Leu Tyr
50 55 60

Asn Tyr Ser Gly Asn Val Thr Pro Tyr Val Ile Thr Thr Asn Glu Met
65 70 75 80

Leu Gly Tyr Val Asn Ile Thr Ser Leu Leu Ala Tyr Asn Arg Glu Ala
85 90 95

Leu Arg Tyr Gly Val Asp Pro Tyr Ser Ala Thr Leu Gln Phe Asn Ile
100 105 110

Val Leu Ser Val Asn Thr Ser Asn Gly Val Tyr Ala Tyr Trp Leu Gln
115 120 125

Asp Val Gly Gln Phe Gln Thr Asn Lys Asn Ser Leu Thr Phe Ile Asp
130 135 140

Asn Val Trp Asn Leu Thr Gly Ser Leu Ser Thr Leu Ser Ser Ser Ala
145 150 155 160

Ile Thr Gly Asn Gly Gln Val Ala Ser Ala Gly Gly Gly Gln Thr Phe
165 170 175

Tyr Tyr Asp Val Gly Pro Ser Tyr Thr Tyr Ser Phe Pro Leu Ser Tyr
180 185 190

Ile Tyr Ile Ile Asn Met Ser Tyr Thr Ser Asn Ala Val Tyr Val Trp
195 200 205

Ile Gly Tyr Glu Ile Ile Gln Ile Gly Gln Thr Glu Tyr Gly Thr Val
210 215 220

Asn Tyr Tyr Asp Lys Ile Thr Ile Tyr Gln Pro Asn Ile Ile Ser Ala
225 230 235 240

Ser Leu Met Ile Asn Gly Asn Asn Tyr Thr Pro Asn Gly Leu Tyr Tyr
245 250 255

Asp Ala Glu Leu Val Trp Gly Gly Gly Gly Asn Gly Ala Pro Thr Ser
260 265 270

Phe Asn Ser Leu Asn Cys Thr Leu Gly Leu Tyr Tyr Ile Ser Asn Gly
275 280 285

Ser Ile Thr Pro Val Pro Ser Leu Tyr Thr Phe Gly Ala Asp Thr Ala
290 295 300

Glu Ala Ala Tyr Asn Val Tyr Thr Thr Met Asn Asn Gly Val Pro Ile
305 310 315 320

Ala Tyr Asn Gly Ile Glu Asn Leu Thr Ile Leu Thr Asn Asn Phe Ser
325 330 335

Val Ile Leu Ile
340

We claim:

1. A recombinant or isolated nucleic acid comprising: (a) a nucleotide sequence comprising a Fusellovirus integration sequence that integrates into a *Sulfolobus* species chromosome; and (b) a nucleotide sequence of interest, wherein the nucleotide sequence of interest is operably linked to a minimal promoter and encodes a protein that is biologically activate at a temperature equal to or more than about 70° C. and/or a pH equal to or less than about 4.0, wherein the minimal promoter is an AraS to tf55 promoter.

2. The nucleic acid of claim **1**, wherein the Fusellovirus is a *Sulfolobus* spindle-shaped virus.

3. The nucleic acid of claim 2, wherein the *Sulfolobus* spindle-shaped virus is SSV1, SSV2, SSV3, SSVL1, SSVK1, or SSVRH.

4. The nucleic acid of claim 1, wherein the protein comprises an export peptide signal at the 5' end.

5. The nucleic acid of claim 1, wherein the protein needs to be expressed, synthesized and/or folded at a temperature equal to or more than about 70° C., 75° C., 80° C., 85° C., or 90° C. in order to be correctly folded and to be biologically active; and/or needs to be glycosylated during or after expression, synthesis and/or folding in order to be biologically active.

6. The nucleic acid of claim 1, further comprising one or more control sequences which permit stable maintenance of the nucleic acid as a vector in a non-*Sulfolobus* host cell.

7. An Archaea host cell comprising the nucleic acid of claim 1 stably integrated into the chromosome of the host cell.

8. The host cell of claim 7, wherein the host cell is hyperthermophilic or acidophilic.

9. The host cell of claim 7, wherein the host cell is capable of growth or is viable at a temperature equal to or more than about 70° C., 75° C., 80° C., 85° C., or 90° C.

10. The host cell of claim 7, wherein the host cell is capable of growth or is viable at a pH equal to or less than about 4.0, 3.5, 3.0, 2.5, or 2.0.

11. The host cell of claim 7, wherein the Archaea is of the genus *Sulfolobus*.

12. A method of genetically modifying a host cell comprising: (a) introducing a nucleic acid of claim 1 into a host cell that is an Archea or acidophilic hyperthermophilic eubacteria, and (b) integrating the nucleic acid into the chromosome of the host cell.

13. A method of expressing a protein of interest in an Archaea, comprising: culturing the host cell of claim 7 in a suitable medium such that the protein is expressed, and optionally isolating the protein from the host cell.

14. The method of claim 13, wherein the protein is a thermophilic enzyme, or enzymatically active fragment thereof, that catalyzes an enzymatic reaction.

15. The method of claim 14, wherein the protein is a cellulase.

* * * * *